MEAN PLATELET VOLUME AN INDICATOR OF ASCITIC FLUID INFECTIONS IN CIRRHOTIC PATIENTS

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CERTIFICATE

This is to certify that this dissertation titled **"MEAN PLATELET VOLUME AN INDICATOR OF ASCITIC FLUID INFECTIONS IN CIRRHOTIC PATIENTS."** has been prepared by **Dr.S.V.SANGEETHA** under my supervision and guidance of **Prof. Dr. R.SABARATNAVEL MD.,** at the Department of General Medicine, Government Kilpauk Medical College, Chennai, during the Academic year 2012-2015, and is being submitted to The TamilNadu Dr.M.G.R.Medical University Chennai in partial fulfillment of the University regulation for the award of the Degree **MD GENERAL MEDICINE BRANCH - I** and her dissertation is a bonafide work.

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DECLARATION

I, **Dr.S.V.SANGEETHA,** solemnly declare that this dissertation **"MEAN PLATELET VOLUME AN INDICATOR OF ASCITIC FLUID INFECTIONS IN CIRRHOTIC PATIENTS."** is the bonafide work done by me at the Department of General Medicine, Government Kilpauk Medical College and Hospital, Chennai, under the guidance and supervision of **Prof.Dr.R.SABARATNAVEL MD.,** Professor and Head of the Department of General Medicine, Government Kilpauk Medical College, Chennai - 600 010. This dissertation is submitted to The Tamil Nadu Dr.M.G.R. Medical University, Chennai in partial fulfillment of the University regulations for the award of degree of **MD GENERAL MEDICINE BRANCH - I** examinations to be held in APRIL 2015.

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CONTENTS

ABBREVIATIONS

AFI	-	Ascitic Fluid Infections
GIT	–	Gastrointestinal Tract
DCLD	-	Decompensated Liver Disease
SBP	-	Spontaneous bacterial peritonitis
MNB	-	Monomicrobial nonneutrocytic bacterascites
CNNA	-	Culture NegativeNeutrocytic Ascites
CNNNA	-	Culture Negative Non-Neutrocytic Ascites
HRS	-	Hepatorenal Syndrome
CTP	-	CHILD TURCOTTE PUGH SCORE
HE	-	Hepatic Encephalopathy
MELD	-	MODEL FOR END- STAGE LIVER DISEASE SCORE
SAAG	-	Serum-ascites albumin gradient.
PMN	-	Polymorhonuclear Neutrophils
SID	-	Selective Intestinal Decontamination
MPV	–	Mean platelet volume

ABSTRACT

MEAN PLATELET VOLUME AN INDICATOR OF ASCITIC FLUID INFECTIONS IN CIRRHOTIC PATIENTS

AIM

Ascitic fluid infection primarily consists of two variants- Spontaneous Bacterial peritonitis and culture negative neutrocytic ascites. Mean platelet volume (MPV) is used as a cheap and non invasive indicator of inflammation in various systemic conditions. So our aim is to analyse whether platelet size alteration would be used as an indicator of ascetic fluid infection in cirrhotic patients.

MATERIALS AND METHODS

A total of 75 patients with ascites with cirrhosis were enrolled in this study. According to ascitic fluid analysis, 29 patients were diagnosed to have ascetic fluid infection. CBC including MPV, ESR were determined for all participants. The ability of MPV in determining ascetic fluid infections were analysed using Pearson chi- square and Fisher extract test.

RESULTS

A statistically significant increase in MPV was observed in cirrhotic patients with AFI compared to cirrhotic patients without AFI ($P<0.005$). A statistically significant observation was observed in respect to MPV, ESR, TC, Ascitic fluid PMN count and culture.

CONCLUSION

Our study shows that MPV is increased in cirrhotic patients with AFI. MPV measurement can be considered as an accurate diagnostic test in predicting AFI, possibly due to ongoing systemic inflammatory response.

KEY WORDS: Ascitic fluid infection, Spontaneous bacterial peritonitis, Mean platelet volume, Cirrhosis, Inflammation.

INTRODUCTION

Ascites is a Greek derivative (askos) and it refers to bag or sack. Ascites is pathologic fluid accumulation within the peritoneal cavity. The most common cause of ascites is cirrhosis with portal hypertension (85%) which occurs within 10years of diagnosing cirrhosis.

Ascites is due to many factors like diseases involving peritoneum (peritonitis, malignancy), liver disease, cardiac failure, hypoproteinemia. In Western countries, cirrhosis is the most common cause of ascites(76%), followed by peritoneal malignancy(14%), cardiac failure(5%), peritoneal tuberculosis(4%)

The development of ascites in cirrhotic patients denotes that the patient progressed to decompensated cirrhosis. There are many complications of cirrhosis like portal hypertension, hepatic encephalopathy, hepatorenal syndrome of which the development of portal hypertension and its manifestation ascites is common and is gaining more importance.

Cirrhosis is a linguistic disorder with indolent course and many patients will be asymptomatic until decompensation. Early and well - compensated cirrhosis usually present as loss of appetite and weight loss, malaise, fatigue and weakness. Decompensated Liver Disease is an end stage liver disorder with

liver fibrosis and with complications like ascites, variceal bleeding, hepatic encephalopathy, SBP and hepatorenal syndrome.

DCLD have poor prognosis with 1 year and 5 year mortality rates of 56% and 80% respectively.

Cirrhosis is an immunocompromised status where both humoral and cell mediated immunity are decreased. So these patients have reduced bactericidal opsonin activity, reduced complements (C3, C4), protein C and fibronectin. The local immune function is also decreased. Due to portosystemic shunting, bacteria and its endotoxins from portal circulation are not cleared by cirrhotic liver. This predisposes the patient to lots of infection. Bacterial infections takes about 37-57% of death in DCLD patients. Nosocomial infections takes about 30-32% and upto 42% of death with variceal bleed. The most common bacterial infections in descending order are spontaneous bacterial peritonitis (15-30%), urinary tract infections (25-29%), pneumonia (18-22%), bacteremia(17%), and soft tissue infections(15%).

In Gastrointestinal variceal bleeding there is disruption of mucosal barrier integrity during bleeding and during invasive procedures. So GIT bleeding is associated with infections in 60% of patients.

Infections trigger cytokine pathway with release of various inflammatory markers and vasoactive mediators that causes increased variceal pressure,

distorted homeostasis leading to further bleeding. So failure to control variceal bleeding within 120 hours are associated with increased rebleeding rates. So early antibiotic prophylaxis prevents infection and episodes of rebleeding and also reduces the need of blood transfusion. The recurrence rate after first episode of SBP are 41% at 5 months, 63% at one year and 72% at 2 years. Early and sensible prophylaxis reduces recurrent rate by 25%. The frequency of ascitic fluid infection among out patient is as low as 0-3.7%. The in- patient mortality varies from 22-45% and mortality rate at one year follow up varies from 57-72%.

AFIs are under diagnosed by conventional culture methods since the Median bacterial concentration is only about one to two organisms per millilitre.

Hence this study is done to detect Ascitic Fluid Infections (AFI) in out patients and in patients with Decompensated Chronic Liver Disease (DCLD) by blood Mean Platelet Volume (MPV) test. With this we can diagnose ascitic fluid infection at the earliest and treating the patients with appropriate antibiotics at the earliest thereby preventing further complications.

AIMS AND OBJECTIVES

1. The usefulness of Blood Mean Platelet Volume in the rapid and early diagnosis of spontaneous bacterial peritonitis in Decompensated Chronic Liver Disease with ascites, so that rapid diagnosis of ascitic fluid infection in cirrhotic patient and starting early antibiotics to reduce the morbidity and mortality of the disease which can be established.
2. To study the incidence and prevalence of Ascitic Fluid Infection in cirrhotic patients of different etiologies.
3. To study the prevalence of ascitic fluid infection among in patients with DCLD.

REVIEW OF LITERATURE

CIRRHOSIS

Cirrhosis means non remitting, progressive, diffuse fibrosis followed by nodular regeneration of liver so that the liver architecture is altered. Long standing injury proceed to progressive injury to the liver resulting in cirrhosis. Persistent wound healing resulting in fibrosis. For clinical manifestation to occur, atleast 80-90% of liver parenchyma should be destroyed. Cirrhosis is an indolent disease with silent course and the patient remain asymptomatic until they reach the stage of decomposition.

CAUSES OF CIRRHOSIS

1. Alcoholism
2. Cardiac cirrhosis
3. Viral induced-Hepatitis B&C
4. Autoimmune hepatitis
5. Non alcoholic steatohepatitis
6. Biliary cirrhosis
    i. Primary biliary cirrhosis
    ii. Primary sclerosing cholangitis
    iii. Autoimmune cholangiopathy
7. Chronic viral hepatitis

8. Inherited metabolic liver diseases
    i. Haemochromatosis
    ii. Wilson disease
    iii. Cystic fibrosis
    iv. α 1 antitrypsin deficiency
9. Cyptogenic cirrhosis

ALCOHOLIC LIVER DISEASE

Alcoholic Liver Disease(ALD) is the most important risk factor for the development of cirrhosis. Individuals who consume large quantity of alcohol for prolonged period, about 60-80gm/day in males and >20gm/day in females over 10 years or longer progress to steatosis of liver in 92% of people. Steatosis can progress to alcoholic hepatitis in 12-37% of people and to cirrhosis in 5-18% of people.

Women are more prone to develop Alcoholic liver disease in a short lifespan due to decreased activity of alcohol dehydrogenase in gastric mucosa and in the liver. Also women have a lean body mass and low threshold for toxic dose when compared to men. This has been attributed to the gender dependent differences in the hepatic metabolism of alcohol.

COMPLICATIONS OF CIRRHOSIS

1. Portal hypertension
    i. Gastro esophageal varices
    ii. Portal hypertensive gastropathy
    iii. Splenomegaly
    iv. Ascites
    v. Spontaneous bacterial peritonitis
2. Hepato renal syndrome
3. Hepato pulmonary syndrome
4. Hepatic encephalopathy
5. Porto pulmonary hypertension
6. Malnutrition
7. Coagulopathies
8. Bone disease
9. Haematological abnormalities
    i. Anaemia
    ii. Hemolysis
    iii. Neutropenia
    iv. Thombocytopenia

ASCITES

Defined as pathological accumulation of fluid in the peritoneal cavity. The most recent theory for the formation of ascitic fluid is **"The peripheral arterial vasodilation hypothesis**". The older theories are Underfilling and overfilling theory.

PATHOGENESIS OF ASCITES

In cirrhotic patients the changes in portal flow and resistance are due to mechanical and vascular factors.

- Mechanical factors include the fibrosis and nodularity with distortion of the vascular architecture and the remodelling of the cirrhotic liver.
- Vascular factors include intrahepatic vasoconstriction, due to increased production of vasoconstrictors like Endothelin-1 which contributes to increased intrahepatic resistance. Both these leads to PORTAL (SINUSOIDAL) HYPERTENSION.

This portal hypertension activates vasodilatory mechanisms. There is increased production of nitric oxide (NO) in the splanchnic circulation which leads to splanchnic and peripheral arterial vasodilation. The later causes decreased levelling of systemic vasculature and produces drop in systemic pressure.

The fall in systemic pressure causes baroreceptor- induced activation of renin- angiotensin pathway with increased activity of sympathetic system and

arginine vasopressin mechanism. This results in renal sodium and water retention to maintain normal homeostasis. Also, splanchnic vasodilation leads to increased lymph production and leakage into peritoneal cavity. Both these events lead to sustained ascitic fluid formation[40].

CAUSES OF ASCITES[14]

Cirrhosis-*85%*

OTHERS-15%

1. Alcoholic hepatitis
2. Cancer (peritoneal carcinomatosis, liver metastasis, etc)
3. "Mixed" ascites
4. Pancreatitis
5. Nephrotic syndrome
6. TB peritonitis
7. Heart failure
8. Acute liver failure
9. Budd-Chiari syndrome
10. Postoperative lymphatic leak
11. Sinusoidal obstruction syndrome
12. Myxoedema.

MIXED ASCITES[61]

Have underlying portal hypertension with cirrhosis along with other conditions like TB or peritoneal carcinomatosis.

SECONDARY PERITONITIS[40,5,20,54]

Look for it when:

1. No diminish in ascitic fluid PMN count 48 hours after antibiotic starting.
2. Two or more organisms shown on culture
3. If in ascitic fluid atleast two (2/3) is seen:

   AF protein >1g/dl.

   AF lactate dehydogenase(LDH)>225mU/ml.

   AF glucose <50 mg/dl.

Antibiotics against anaerobes and enterococci have to be added.

TUBERCULOUS PERITONITIS

Abdominal tuberculosis is the sixth most frequent site[49] of tuberculosis.

Peritoneal TB occurs in three types:

1. Fibrotic type.
2. Encysted (loculated) type.
3. Wet type with ascites.

Macroscopically it is straw coloured and an exudate (protein>3g/L).

The total cell count is 500-2000 cells/mm3 with predominant of lymphocytes (70%). Lymphocytosis of ascitic fluid means that the lymphocytes account for >30% of total AF cell count[39].

Sometimes PMNs may be abundant (>250/mm3) early in the disease and this can lead to misdiagnosis as SBP[2,39,45].

The SAAG has a gradient of <1.1g/dl.

The adenosine deaminase (ADA) of >33U/L has a sensitivity of 98% and specificity of 100% in non-cirrhotic patients[4].

The yield of tubercle bacilli on smear and culture is low and large amounts of fluid (about 1L) has to be used for centrifuge and the deposit is inoculated on LJ medium. The time taken for growth of tubercle bacilli is usually 6-8 weeks[2,29,45].

GRADING OF ASCITES

THE INTERNATIONAL ASCITES CLUB[40]

Grade one -Ultrasound detected.

Grade Two -Abdominal distention.

Grade Three -Tense ascites

TYPES OF ASCITES

1. Uncomplicated Ascites- Ascitis in the absence of infection/ HRS.
2. Refractory ascites can be prevented with drug treatment after therapeutic paracentesis.
3. Diuretic- Resistant ascites - Ascites persists even after high dose or maximum dose of diuretic treatment.
4. Diuretic- Intractable ascites - diuretics causing side effects leading to improper treatment.

ASCITIC FLUID INFECTIONS (AFI).

The most common complication of cirrhosis with portal hypertension is the ascitic fluid infection (31%) .

Ascitic fluid infections (AFIs) has been classified into five variants based on analysis of the following parameters-

- Polymorphonuclear leukocyte (PMN) count
- Culture growth and
- Mode of entry of organism into the fluid[66].

CLASSIFICATION OF ASCITIC FLID INFECTION

1. Spontaneous Bacterial Peritonitis
2. Monomicrobial Non-Neutrocytic Ascites
3. Culture Negative Neutrocytic Ascites
4. Polymicrobial Bacterascites
5. Secondary Bacterial Peritonitis

Criteria for diagnosing Spontaneous Bacterial Peritonitis

1. PMN count >250cells/mm^3.
2. A positive ascitic fluid culture.

Criteria for diagnosing Monomicrobial Non-Neutrocytic Ascites

1. PMN count < 250cells/mm^3.
2. A positive ascitic fluid culture for a single organism.

Criteria for diagnosing Culture Negative Neutrocytic Ascites

1. PMN count is 250cells/mm^3.
2. Ascitic fluid culture - no organism

Criteria for diagnosing Polymicrobial Bacterascites

1. PMN count < 250cells/mm^3.
2. Ascitic fluid culture – multiple organisms

Criteria for diagnosing Secondary Bacterial Peritonitis

1. PMN count is 250cells/mm^3.
2. Ascitic fluid culture – multiple organisms
3. Intra abdominal surgically treatable primary infection

SPONTANEOUS BACTERIAL PERITONITIS

HISTORY

It is of historical interest that ***Ludwig von Beethoven*** is probably the first patient known by the name to have had SBP, especially since the clinical description of his case had been written 135 years before this syndrome was first described.

Kerr et al & Conn, printed papers which explained ascitic fluid infections (AFIs) in the absence of contiguous or intra-abdominal source of infection[10].

Conn in 1984 was the one coined the term Spontaneous Bacterial Peritonitis (SBP)[3].

Runyon who has done several works in SBP suggests that we have to now drop the term "SPONTANEOUS" since the pathogenesis has been studied and worked out[25].

INTRODUCTION

Spontaneous bacterial peritonitis is an infection of ascitic fluid in the absence of any intra-abdominal or surgically treatable source of infection. It is diagnosed by a positive culture and ascitic fluid PMN cell count of $\geq 250/mm^3$, in the absence of a surgically treatable intra-abdominal source of infection.

Although SBP has been described in many different clinical settings, like nephrotic syndrome, malignant metastatic disease, post necrotic cirrhosis, chronic active hepatitis, acute viral hepatitis, congestive heart failure, systemic lupus erythematosis (SLE) and lymphedema and also in patients with no underlying disease, most episodes develop in adults in conjunction with cirrhosis of the liver.

PREVALANCE

Ascitic fluid infection is the most frequent infectious complication among patients with cirrhosis with ascites comprising 31% of all bacterial infections in the human body.

The prevalence of SBP in the past was relatively low 5% to 10% in cirrhotic patients with ascites. However the recent studies using newer diagnostic criteria

and improved culture techniques have estimated a prevalence of 10% to 30% among inpatients and 3.5% among outpatients.

RISK FACTORS

- Severity of the liver disease-Child-Pugh class C patients
- Urinary tract infection and asymptomatic bacteruria[14]
- Serum total bilirubin level more than 2.5 mg/dl
- Gastrointestinal bleeding
- Increased prothrombin time[54]
- Increased liver enzymes[54]
- Previous episodes of SBP[21]
- Ascitic fluid protein level <1g/dl

MICROBIOLOGY

Bacteria most commonly isolated from ascitic fluid in patients with SBP are usually those of the normal intestinal flora. More than 92% of all cases are monomicrobial with aerobic gram negative bacilli. This is being responsible for more than two third of cases.

Escherichia coli accounts for nearly half of these cases followed by *Klebsiella spp* and other gram negative bacteria. Twenty-five percent of cases are caused by gram positive organisms with *Streptococcus spp* being the most common. In bacterial peritonitis associated peritoneal carcinomatosis, the microorganisms

isolated are those which are not usually known to cause SBP and quite virulent, for example, *Salmonella spp*. SBP is rarely caused by anaerobic organisms, so their presence in ascitic fluid should raise suspicion due to some other cause. In other cases, the bacteria may reach the ascitic fluid from the urinary or respiratory tracts.

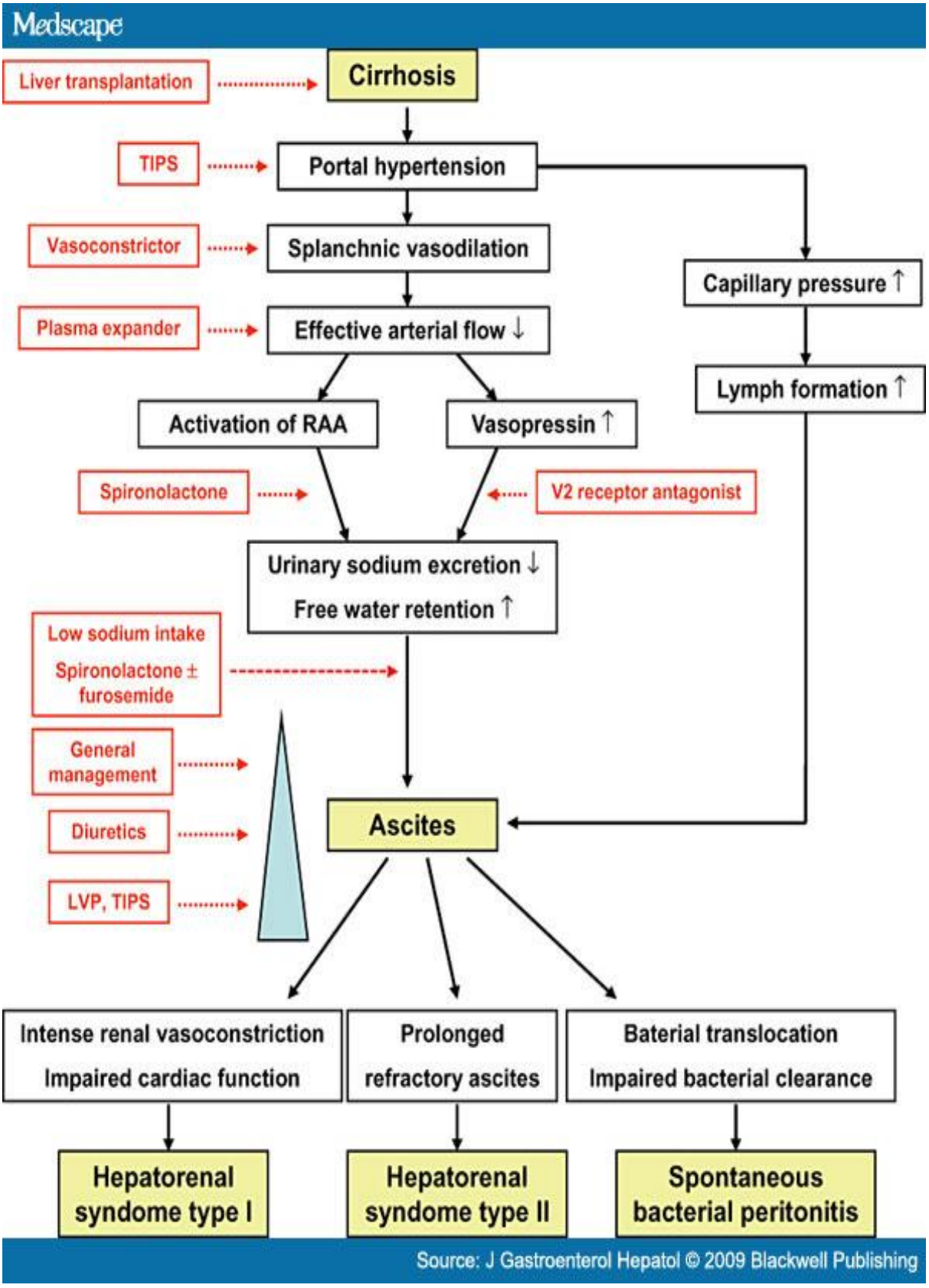
PATHOGENS IN ASCITIC FLUID INFECTION

1. Escherichia coli
2. Klebsiella pneumoniae
3. Streptococcus pneumonia
4. Streptococcus viridans
5. Staphylococcus aureus
6. Miscellaneous gram positive and gram negative organisms.

PATHOGENESIS

GENERAL CONCEPT

Although the pathogenesis of SBP is not completely understood, it is thought that it occurs as a consequence of translocation of bacteria across the gut wall to the intestinal lymph nodes, with subsequent bacteremia and infection of the ascitic fluid.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Portal hypertension
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Capillary pressure ↑
Plasma expander
Effective arterial flow ↓
Lymph formation ↑
Activation of RAA
Vasopressin ↑
Spironolactone
V2 receptor antagonist
Urinary sodium excretion ↓
Free water retention ↑
Low sodium intake
Spironolactone ± furosemide
General management
Diuretics
LVP, TIPS
Ascites
Intense renal vasoconstriction
Impaired cardiac function
Prolonged refractory ascites
Baterial translocation
Impaired bacterial clearance
Hepatorenal syndome type I
Hepatorenal syndome type II
Spontaneous bacterial peritonitis
Source: J Gastroenterol Hepatol © 2009 Blackwell Publishing

It is generally accepted that it involves three major steps:

- Passage of bacteria from the intestinal lumen, or from other sources in a lower proportion of cases to the systemic circulation.
- Bacteremia secondary to the impairment of the reticulo endothelial system (RES) phagocytic activity.
- Infection of ascites due to defective bactericidal activity of the ascitic fluid.

Studies in experimental animals with cirrhosis suggest that the first step in the passage of bacteria from the intestinal lumen to the ascitic fluid is the colonization of mesenteric lymph nodes, a process known as **bacterial translocation**.

Evidences supporting this mechanism includes:

- The isolation of gram-negative bacilli from mesenteric lymph nodes in a large proportion of cirrhotic rats with ascites
- Isolation of the same bacteria from lymph nodes and ascites in most cases
- The presence of histologic abnormalities in the intestinal wall, such as submucosal edema involving the cecum and ileal lymphangiectasia. All these may facilitate the translocation process.

Transmigration across the gut wall is the most likely mechanism by which bacteria from the intestinal lumen reaches the mesenteric lymph nodes. Intestinal bacterial overgrowth and impaired small bowel motility, which are

common in both experimental and human cirrhosis, may facilitate bacterial translocation.

THE POSSIBLE ROUTES OF ENTRY OF BACTERIA

1. Organisms can come directly from the gastrointestinal tract, or from the blood stream.
2. The rarest route is through the Fallopian tubes. This route of entry has been implicated by **McCartney** to explain the predominance of girls with primary peritonitis. (5)

The most common causes of bacterial peritonitis:

- Perforations of ulcers of upper gastrointestinal tract.
- The rupture of abdominal viscera, usually the appendix.

Although perforations of the gastrointestinal tract may be clinically silent, and even when silent they usually exhibit pneumoperitoneum. Under certain conditions bacteria may enter the peritoneal cavity by traversing the intact intestinal wall66.

BACTERIAL OVERGROWTH

Bacterial overgrowth occurs from

- Overgrowth of a single species of indigenous bacteria in the intestinal tract.

- Immunosuppressive conditions like HIV, diabetes.
- Thermal injuries in which large segments of skin are burned,
- Haemorrhagic, hypotensive shock, i.e., insufficient blood supply to the gastrointestinal (GI) tract.
- In addition, specific disorders of the Gastrointestinal tract, such as intestinal or biliary obstruction or portal hypertension, may all give rise to Bacterial overgrowth[31].

ROLE OF HEPATIC LYMPHATICS

It is possible that the hepatic lymphatics themselves may be involved in the pathogenesis of SBP. Hepatic lymph is the key to the formation of ascites. In cirrhotic patients when there is hepatic venous outflow obstruction, the production of hepatic lymph is increased resulting in the formation of ascites, largely due to the exudation of hepatic lymph directly into the peritoneal cavity[31].

THE FACTORS PRONE TO DEVELOP SBP

Failure of hepatic removal of bacteria from the blood stream. **McIndoe** described the extrahepatic portal-systemic collateral networks that shunt portal venous blood around the liver.

These portal -systemic shunts have been shown to diminish the hepatic clearance of ammonia and other nitrogenous substances absorbed from the gastrointestinal tract. By these portal-systemic anastomoses, the circulating bacteria bypass the hepatic reticuloendothelial filtering system, which has been shown to be the major site of removal of bacteria from the blood. Decreased hepatic removal of circulating bacteria tends to perpetuate bacteremia and thus afford circulating organisms, a greater opportunity to cause infections at susceptible sites such as ascitic fluid.[41,42]

Normally the portal venous blood is aseptic. In case of migration of bacteria from infected lumen , they are getting trapped and removed by the liver. Cirrhotics have increased and abnormal bowel flora[41]. Bacterial overgrowth is increased in cirrhosis by delayed intestinal transit, decreased luminal IgA and bile salts.[66]

DELAYED INTESTINAL MOTILITY

Normal distal movements of the luminal contents by peristalsis helps to avoid colonization and multiplication of bacteria in the upper intestine. This movement is facilitated by MMC (MIGRATORY MOTOR COMPLEX) -the "intestinal housekeeper". The complete or partial absence of the phase III activity of MMC results in bacterial overgrowth[17]. In cirrhosis, there is

increase in bacterial colonization of the small bowel (31-53%) with bacteria from the large bowel[38].

INTESTINAL MUCOSAL BARRIER

SECRETORY MECHANISM (1st LINE DEFENCE)

The goblet cells of intestinal epithelium secret mucins that acts as electro- negative charged layer preventing the direct contact between bacteria and intestinal membrane. In cirrhotic patients with sepsis there is an elevated permeability of intestinal mucosa due to oxidative stress, elevated Nitric Oxide, endotoxins, various proinflammatory cytokines, and enterocyte mitochondria malfunction .[38]

IMMUNOGLOBULIN A

70% of body's immunoglobulin production is IgA. In cirrhotics patients there is diminished production of mucosal IgA[17,38.12].

BILE'S TROPHIC EFFECT

Bile inhibits intestinal bacterial overgrowth;

Bile has detergent action and anti-adherence properties, endotoxin removal, trophic effect for intestinal mucosa with decreased epithelial bacteria internalisation. The quantity of bile acids in liver disease is diminished due to

decreased secretion and accentuated deconjugation of bile by intestinal flora. It aids in bacterial translocation caused by endotoxins[17,38].

THE PHYSICAL MECHANISM (2nd LINE DEFENCE)

INTESTINAL EPITHELIAL STRUCTURE

Tight junctions between the cells located at the apicolateral surface of the epithelium inhibits the transport of bacteria or its lipopolysaccharide.

In liver disease there is widening of intercalated cells, decrease in the number of crypts and villus, Vasodilation, oedema of muscularis mucosae and fibromuscular proliferation. All these factors breaks the integrity of the normal epithelium[38].

NATURAL ANTIBIOTIC SECRETION

- Paneth cells in the jejunal and ileal crypts produce - phospholipase A2, defensins, and lysozyme, cryptidin related signal peptides, which have natural antibiotic property.
- Small intestine epithelial cells and Colonic epithelial cells secrete defensins that defend against commensal bacteria.

In chronic liver disease secretion of these substances with antimicrobial activity is reduced.[13]

GUT ASSOCIATED LYMPHOID TISSUE.

Four components

1. Lymphocytes from the lamina propria.
2. Intraepithelial lymphocytes
3. Mesentric lymph nodes (MLN)
4. Peyer's patches

When the Bacteria interact with the structures in the Gut Associated T Lymphocytes, there is multiplication of lymphocytes in the germinal centers of reticuloendothelial system and so the mucosal immunoglobulin secretion gets elevated [38].

The primary immune response was associated with monocytes. By its interaction of ***PRR*** *-PATTERN RECOGNITION RECEPTOR with specific bacterial ligands* ***PAMPs*** *-PATHOGEN ASSOCIATED MOLECULAR PATTERNS,* the antigens are taken up by the dendritic cells through the local antigen presenting cells (APCs) –***DIRECT MECHANISM*** and by M cells which overtake the antigen by endocytosis- ***INDIRECT MECHANISM*** [38].

Microbial peptides are presented by the Antigen presenting cells to the B & T lymphocytes. This will result in the secretion of mucosal IgA (or IgG) or its transformation into Th1 and Th2 cells. On exposure to the antigen, the T

lymphocyte from the Peyer's patches[14] move towards lamina propria and gets tranformed into CD8 T – lymphocytes. Impaired primary and adaptive immune response occurs in DCLD[38,17]

BACTERIAL TRANSLOCATION

Portal hypertension causes venous stasis, hypoxia of the mucosa and oxidative stress induced cytotoxic damage[28,30]. This leads to splanchnic dilatation with Mucosal congestion and Bowel Oedema leading to altered bowel permeability and bacterial translocation to mesentric lymph nodes[40]. Gram negative bacteria are more adapt than Gram positives and anaerobes in translocation[66].Bacteria generally do not migrate directly from the lumen into ascitic fluid. It happens if there is a loss of mucosal integrity.

Anaerobes are present in excess in gut flora which translocate only in intestinal mechanical injury and are occasionally isolated from ascetic fluid in SBP[66,17].

More virulent organisms and Escherichia coli strains with greater adherence to intestinal mucosa translocate more precisely [21].

INVASION OF ASCITIC FLUID AND BACTEREMIA

Splanchnic and systemic vascular dilatation results in hyperdynamic circulatory state with elevated cardiac output and drop in blood pressure[21]. Due to the high circulatory state, due to spilling over of the organisms from mesenteric lymph nodes into systemic circulation results in bacteremia.[15]Due to the diminished phagocytosis of reticuloendothelial system, the bacteria stays uncleared from the circulation for a long period[66]. In cirrhotic patients due to the presence of intra and extra hepatic shunts the bacteria never come into alignment with the Kuffer cells and thus the bacteremia increases[77]. Bacteremia results in oozing of infected fluid through Glisson capsule and oozing of infected interstitial fluid from intestinal capillaries leads to colonisation of ascitic fluid.

SBP AND BACTERASCITES

Opsonins level and C3 complement level are decreased in DCLD. Low protein concentration (<1g/dl) have positive correlation with decreased opsonic activity.

Opsonins and macrophages were not able to kill the bacteria and so the neutrophils are allowed to do the killing process. SBP occurs, since there is

impaired neutrophil function or qualitative neutrophil abnormalities.[40,58,66,17].

SEPSIS AND SYSTEMIC INFLAMMATORY RESPONSE SYNDROME.

Lipopolysaccharides and peptidoglycans in the bacteria can trigger the TLR receptors[16] that leads to the production of various pro-inflammatory cytokines. This leads to inadequate tissue perfusion, multi-organ failure (MODS), refractory hypotension, sepsis syndrome pathways finally results in death.[21,42,58].

SIGNS AND SYMPTOMS OF SBP

The most common reported are:

- Fever(68%)
- Abdominal pain(68%)
- Hepatic encephalopathy(53%)
- Ileus or Diarrhea(31%)
- Vomiting(20%)
- About 14% of patients with SBP are asymptomatic[37,63].

HEPATORENAL SYNDROME[4]

The annual incidence of HRS in patients with ascites is 10%. There is no major change in renal biopsy and is completely relieved by liver transplantation.

New Diagnostic criteria of the hepatorenal syndrome[12].

- Cirrhosis with ascites
- Serum creatinine >1.5 mg/dL (133μmol/L)
- No improvement in serum creatinine (decrease to a level of 1.5 mg/dL or less) after at least 2 days of diuretic withdrawal and volume expansion with albumin 1 g/kg of body weight per day up to a maximum of 100 g/day
- Absence of shock
- No current or recent exposure to nephrotoxic drugs
- Absence of parenchymal kidney disease as indicated by proteinuria of >500 mg/day, hematuria (>50 red blood cells per high power field), and/or abnormal renal ultrasonography

Adapted from Salerno et al. [12].

HRS TYPE 1

Renal failure with increased serum creatinine reaching >2.5mg%[12] in <2 weeks. It may occur spontaneously or it can be precipitated by bacterial infections, gastrointestinal bleeding or acute hepatitis super imposed on cirrhosis. It develops in 30% of inpatients with SBP[32].

HRS TYPE 2

Moderate and steady decrease in renal function over months (serum creatinine < 2.5 mg/dl). There is severe ascites with poor or no response to diuretics (refractory ascites).

CHILD TURCOTTE PUGH (CTP) SCORE[61]

Initially it was used to prognosticate the short term mortality, it is now used to assess the prognosis and the requirement for liver transplantation. It contains parameters five parameters like total bilirubin, serum albumin, PT-INR, ascites and hepatic encephalopathy.

A : 5-6 points.

B : 7-9 points.

C : 10-15 points

S.No	VARIABLE	1POINT	2POINTS	3POINTS
1.	Total bilirubin	<2mg/dl	2-3mg/dl	>3mg/dl
2.	Albumin	>3.5g/dl	2.8-3.5g/dl	<2.8g/dl
3.	INR	<1.7	1.7-2.2	>2.2
4.	Ascites	No	Mild(Medically controlled)	Severe(Poorly controlled)
5.	Hepatic Encephalopathy	No	GradeI-II (Medically controlled)	GradeIII-IV (Poorly controlled)

MODEL FOR END- STAGE LIVER DISEASE (MELD) SCORE[50]

Includes three lab objectives

- International normalized ratio(INR),
- Serum creatinine and
- Serum bilirubin.

MELD=9.57×loge(creatinine)+3.78×loge(totalbilirubin)+11.2× loge(INR) + 6.43. MELD is better than CTP in evaluating the mortality following variceal bleeding. Addition of the renal parameter creatinine explains its importance in evaluation of mortality risk. CTP has more variabilites than MELD. Also MELD has wider possible scores and offers more weightage than CTP. Patients with high MELD score (>15) are more prone for infections and mortality than patients with low MELD score (<15).

RECOMMENDATIONS FOR DIAGNOSIS OF AFIs.

The AFIs clinically present with single or multiple symptoms. Considerable elapse of time leads to raised morbidity and mortality. The diagnosis is primarily on ascitic fluid analysis[5,40,3].

INDICATIONS FOR DIAGNOSTIC PARACENTESIS[3,5,37]

- New onset ascites.
- Localising signs of peritonitis mentioned above.[22]
- At the time of each admission to hospital.
- In gastrointestinal bleeding prior to antibiotic prophylaxis.
- Laboratory test (LFT) abnormalities.
- Rapid impairement in renal function.

Paracentesis is safe despite the predictable coagulopathy in cirrhotic patients.

COMPLICATIONS OF PARACENTESIS

- Prolonged leakage – most common
- Abdominal wall haematoma-2%
- Haemoperitoneum –0.02%
- Iatrogenic infections- 0.02% (0.7%),
- Visceral perforation- 0.7%

ASCITIC FLUID LABORATORY DATA

TESTS ROUTINELY DONE

- Cell counts with differential count.
- Culture.
- Gram's stain[23]
- Total protein including albumin
- Lactate dehydrogenase
- Glucose
- Amylase

These tests also help to readily differentiate and identify the various etiologies of ascites besides from portal hypertension. The SAAG (Serum-ascites albumin gradient) helps in indentifying the presence of portal hypertension.[14]

CORRECTED SAAG

In serum hyperglobulinemia of >5gm/dl, narrow SAAG gradient occurs in 1% of ascitic fluid specimen.

CORRECTED SAAG = Uncorrected SAAG × 0.16 × (serum globulin [g/dl] + 2.5)

CAUSES OF LOW GRADIENT (SAAG<1.1g/dl) ASCITES[14]

- TB-AF LDH (<250 U/ml) and low glucose level.
- Pancreatic ascites
- Malignancy induced ascites-AF LDH and high glucose level.
- Biliary ascites
- Renal ascites

MACROSCOPY: GROSS APPEARANCE OF ASCITIC FLUID

- Crystal clear- protein level decreased
- Transparent and yellow-Non- neutrocytic ascites (PMN<250/mm3)
- Cloudy- Cells value of 5000/mm3 is cloudy, and greater than 50,000/mm3 appears mayonnaise.
- Bloody- Ascitic Fluid RBCs of 10,000/mm3 is the maximum.
    - RBC >20,000/mm3 is hepatocellular carcinoma.
- Chylous/milky – Ascitic fluid with Triglyceride >200mg%
- Dark brown- Biliary concentration more than that of serum, due to biliary perforation.

IMPORTANCE OF CELL COUNT

The ascitic fluid POLYMORHONUCLEAR LEUKOCYTES count (maximum> 250 cells/mm3) is the efficient test for diagnosis of AFI. But PMN

count above this value can also be found in bleeding into the ascites, peritoneal carcinomatosis and pancreatic ascites [66]. In tuberculous or malignant ascites, lymphocytes will increase.

MANUAL VS AUTOMATED COUNTING

The laboratory should perform the cell count within 60 minutes. The manual count is error-prone and subjective and it also retards the start of ever needed empirical antibiotic therapy[3,13,69]. Automated cell counters are ideal but the manufacturers do not recommend it for fluids other than blood[13]. This can be useful if further validated[14].

GRAM STAINING

Gram staining is not recommended in the diagnosis of SBP. Gram stain is insensitive in detecting SBP and is associated with a high false positive rate.

DIPSTICK TEST

Testing of ascitic fluid using leukocyte esterase dipsticks is simple and Inexpensive method and can be performed at the bedside. The results are available within a maximum of 2 minutes. It is a useful test in the area which is less equipped or understaffed and where culture is not available or takes too long time to get results.

ASCITIC FLUID LACTOFERIN

Measuring ascitic fluid lactoferin, which is a proposed marker of SBP, was done, involving 148 patients with ascites. Sensitivity and specificity were 96 and 87 percent, respectively, using a cut-off level of 242 ng/mL.

However more studies for validation of this test are needed.

RELAVENT ADDITIONAL INVESTIGATIONS[3,5]

1. Blood cultures associated with the ascitic fluid cultures- positive in atleast 1/3 rd of cases[26].
2. Complete blood count
3. WBC count may be low inspite of the presence of SBP due to Hypersplenism[57].
4. Urine analysis and urine culture-asymptomatic bacteriuria is an independent risk factor[14].

TREATMENT

Spontaneous Bacterial Peritonitis –

Cefotaxime 2gm IV every 8th hourly Metronidazole 500mg IV 8th hourly empirically followed by specific antibiotics according to culture and sensitivity.

PROPHYLAXIS

SELECTIVE INTESTINAL DECONTAMINATION

(SID)[23,36,37]

Norfloxacin is recommended :

Poor intestinal absorption and it rapidly diffuses into the ascitic fluid. Preserves anaerobes and prevents gut colonization by pathogenic bacteria. Strong activity against gram negative bacteria.

INDICATIONS

Patient with Gastrointestinal bleeding

- Norfloxacin 400mg BD for 7 days.

Ascitic fluid protein <1 gm% Previous history of SBP

Newer quinolones are preferred since apart from eliminating gram negative bacteria, it decreases bacterial adhesion to mucosa, and they also stimulate bactericidal capacity of PMNs.

Patients who survive an episode of SBP have 41 to 71% chance of relapse in the forecoming 13 months. Hence, long term administration of quinolones is advocated for these patients till they are having symptoms and signs of ascites, transplantation or death.

But this approach selects quinolone resistant GNB and trend towards infection caused by GPC. For patients on quinolone prophylaxis who develop an SBP episode, third generation cephalosporins are the best option.

DISEASE SEVERITY AND CLINICAL OUTCOME

Studies have shown that the mortality rate due to spontaneous bacterial peritonitis in hospitalized patients in the past was around 80% to 90%. However, widespread use of diagnostic paracentesis with the higher index of suspicion of infection, with various diagnostic criteria, together with use of better and safer antibiotics, has significantly improved the short-term prognosis in SBP patients. Currently, there are essentially no deaths as a result SBP, provided it is detected and treated before the development of its complications likes hock or renal failure.

Though the prognosis of SBP has improved in recent years with the advent of effective antibiotics and quick intervention, the long-term prognosis of SBP remains extremely poor among survivors of an episode of SBP, due to the manifestation of severe impairment of liver function.

Probabilities of survival for 1 and 2 years are in the range of 20% and 30% respectively and in some cases 30 to 50%. Liver transplantation should be considered for patients who survive an episode of SBP . SBP is deadly and reports since 1970 shows that, the mortality rate exceeded 90% .

Factors associated with poor outcome include several indicators of poor liver function such as the development of renal failure, hepatic encephalopathy,

high levels of serum bilirubin, and upper gastrointestinal bleeding. The development of renal impairment after the diagnosis of SBP is probably the strongest independent predictor of death.

In a study by Follo et al. in 252 consecutive episodes of SBP, the mortality rate was 100% when associated with progressive renal impairment, 31% when associated with stable renal impairment, and only 7% in those without renal impairment.

PLATELETS

HISTORY

Platelets are small anucleate cells playing a critical role in haemostasis and Thrombosis[70]. Platelets were described by **ADDISON** in 1841 as –extremely minute granules in clotting blood and were termed platelets by ***Bizzozero***, who observed their adhesive qualities as increased stickiness when a vessel is damaged.

PLATELET FORMATION

MEGAKARYOCYTE DEVELOPMENT.

Megakaryocytes are the myeloid cells(constituting less than 1% of these cells) residing primarily in the bone marrow but also found in the lung and peripheral blood. In early development, megakaryopoiesis occurs within the fetal liver and yolk sac. Megakaryocytes arise from pluripotent stem cell that develop into 2 types of precursors, burst-forming cells and colony-forming

cells, expresses the CD34 antigen[72]. Thrombopoietin (TPO), the primary regulator of thrombopoiesis, is currently the only known cytokine required for megakaryocytes to maintain a constant platelet mass. The other regulators include IL-3, IL-6, and IL-11, and are not essential for megakaryocyte maturation[72].

THE FLOW MODEL OF PLATELET FORMATION.

Platelets are assembled along essential intermediate pseudopodial extensions, called proplatelets, generated by the outflow and evagination of the extensive internal membrane system of the mature megakaryocyte **(proplatelet theory).** The proplatelet and platelet formation process generally commences from a single site on the megakaryocyte where 1 or more broad pseudopodia form. Over a period of 4–10 hours, the pseudopodial processes continue to elongate and become tapered into proplatelets with an average diameter of 2–4 μm. The generation of additional proplatelets continues at or near the original site of proplatelet formation and spreads in a wavelike fashion throughout the remainder of the cell until the megakaryocyte cytoplasm is entirely transformed into an extensive and complex network of interconnected proplatelets.

PLATELET LIFE SPAN

The average lifespan of platelets is 7-10 days.

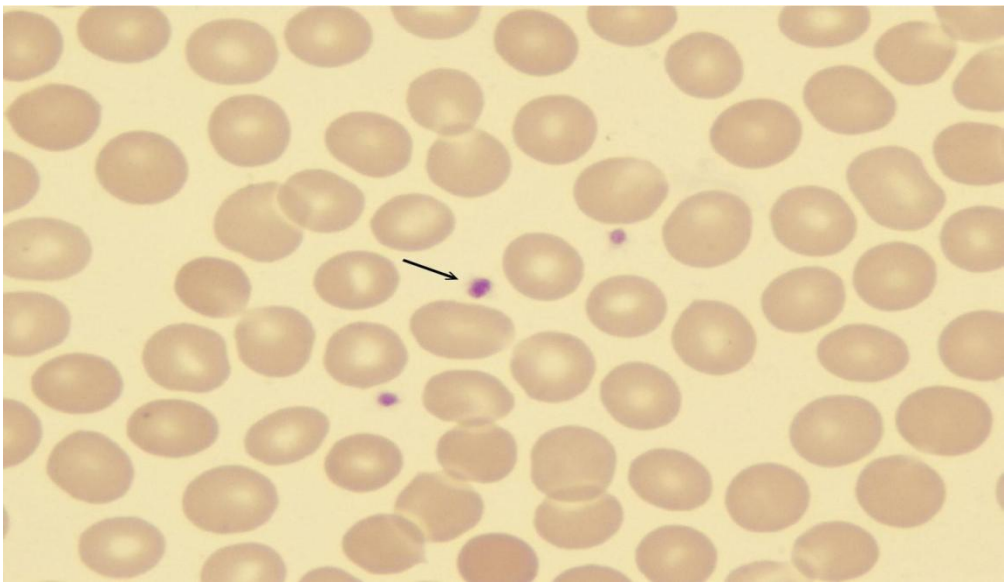
Platelets are lost from circulation by two mechanisms:

- Senescence
- Random removal in endothelial supportive functions of a fixed fraction of platelets amounting $7.1x10^9$/l/day.

Senescent platelets are removed primarily by macrophages in the spleen, although the larger blood flow through the liver allows severely damaged platelets to be removed more quickly by hepatic macrophages.

LIGHT MICROSCOPY

Wright-stained smears reveals platelets are small, anucleate fragments with occasional reddish granules, measures approximately 2μm in diameter with a volume of approximately 8fl[72] and with considerable variation in size and shape.



ELECTRON MICROSCOPY AND SUB-CELLULAR FEATURES

Platelets exist in two distinct forms:

Resting form - baseline metabolic activity

Activated form - agonist stimulation (i.e., response to thrombin).

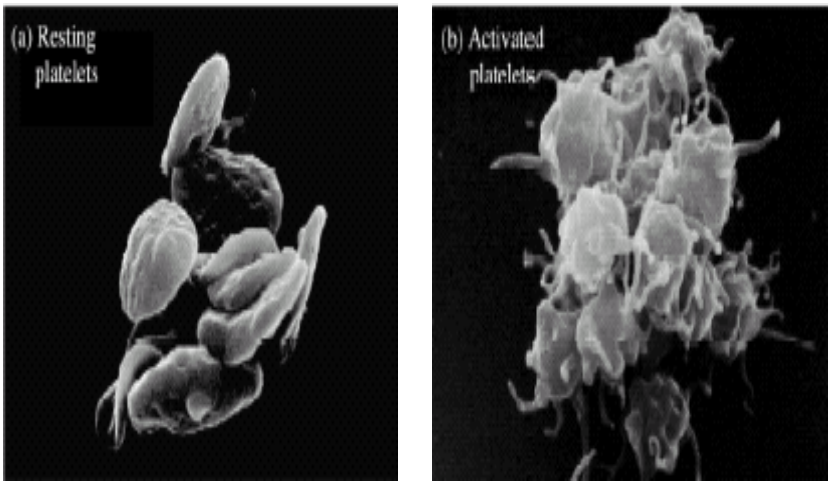


Figure. Resting and activated platelets*

Platelets change their structure during the resting to activated transition.

Platelet structure is classified into four general areas:

- Platelet surface.
- Membrane structures.
- Cytoskeleton.
- Granules.

PLATELET SURFACE

Plasma Membrane: 20nm thick trilaminar structure.[73] The membrane is exceptionally complex in composition, distribution, and function. It

incorporates a number of glycoproteins and lipids into its phospholipid bi-layer and integrates a variety of events such as permeability, agonist stimulation, and platelet adhesion, activation/secretion, and aggregation.

Glycocalyx: A fuzzy layer of lipids, sugars, and proteins.15-20 nm thick. It coats the outer surface of the platelet plasma membrane. This layer provides a transfer point for plasma proteins such as fibrinogen as they are taken up into secretory granules by endocytosis[75]. The glycocalyx contains glycoproteins, glycolipids, mucopolysaccharides, and absorbed plasma proteins. It produces a net negative surface charge mainly due to sialic acid residues on certain protein such as gpIb[76]. This protein is thought to minimize the attachment of circulating platelets to each other and to vessels

PLATELET MEMBRANOUS SYSTEMS

Platelets membrane have high content of actin and they have contractile response during activation. Similar muscle like qualities found in the two membranous systems of platelets, the SCCS and the dense tubular system, which resemble transverse tubules and sarcotubules, respectively [76]

PLATELET CYTOSKELETON

Both the shape of platelets and their ability to contract and spread depend on the cytoskeleton[77].The cytoskeleton can direct platelet shape change, send out extracellular extensions, collect and then extrude secretory granules, and affect surface activity. These functions are

performed by three distinct structures:

1. The membrane skeleton, which buttresses the inner side of the plasma membrane.
2. The mass of actin and intermediate filaments, which fills the cytoplasm.
3. The circumferential microtubule band, which encircles the substance of the platelet to produce the resting disclike form.

PLATELET GRANULES AND ORGANELLES

PLATELET GRANULES

Normal platelet function appears to require some amplification of any given stimulus to obtain an appropriate response. The platelets possess secretory granules and mechanism that serve this purpose by releasing additional stimulatory materials, that are previously sequestered within the resting platelet.

Two main secretory granules, the α-granules and the dense bodies contain highly reactive contents adenosine diphosphate (ADP) and fibrinogen respectively. Platelet granule secretion begins with a dramatic increase in platelet metabolic activity, stimulated by calcium release and results in increased adenosine phosphate (ATP) production

Table 1 Contents of the three different granule subpopulations (α-granules, dense granules, and lysosomes) of platelets.[1]

Dense granules	*Nucleotides*
	Adenine: ATP, ADP
	Guanine: GTP, GDP
	Amines
	Serotonin
	Histamine
	Bivalent cations
α-granules	*Adhesion molecules*
	P-selectin (CD62P)
	Platelet endothelial cell adhesion molecule-1 (PECAM-1/CD31)
	Glycoprotein IIb/IIIa (GPIIb/IIIa, $\alpha_{IIb}\beta_3$ integrin, CD41/CD61)
	von Willebrand factor (vWF)
	Thrombospondin-1 (TSP1)
	Vitronectin, Fibronectin
	Mitogenic factors
	Platelet-derived growth factor (PDGF)
	Vascular endothelial growth factor (VEGF)
	Transforming growth factor-ß (TGF-ß)
	Coagulation factors
	Fibrinogen, Plasminogen, Protein S, Kininogens
	Factors V, VII, XI, XIII
	Protease inhibitors
	C1 inhibitor
	Plasminogen activator inhibitor-1 (PAI-1)
	Tissue factor pathway inhibitor (TFPI)
Lysosomes	*Glycosidases*
	Proteases
	Cationic proteins

ORGANELLES

Microperoxisomes: are small 90 nm in diameter granules, demonstrable with alkaline diamino benzidine due to their catalase activity. It may participate in the synthesis of platelet-activating factor, but its ultimate fate within the platelet cytoplasm is unknown[74]. Coated vesicles are 70 to 90 nm in diameter. The polyhedral surface coat is composed of clathrin,.

Mitochondria: Mitochondria in platelets are smaller size. There are approximately seven per human platelet. They serve as the site for the actions of the respiratory chain and the citric acid cycle[78]. Glycogen is found in small particles or in masses of closely associated particles, play an essential role in platelet metabolism.

PLATELET FUNCTION AND INFLAMMATION

Hemostasis and inflammation are closely linked and are often activated concomitantly [80] . In response to inflammatory stimuli, circulating leukocytes roll and then adhere on the endothelial cells and finally migrate into the surrounding tissues. In response to vascular damage, circulating platelets adhere to the subendothelial tissues and then recruit more platelets to form aggregates that function as procoagulants [80]. These processes are mediated by cell adhesion molecules.

Platelet adhesion receptors are classified into four groups based on their molecular structure:

1. Selectins (P-selectin),
2. Integrins (e.g. GPIa-IIa, GPIIb/IIIa),
3. Leucine-rich glycoproteins (GPIb-V-IX and GPIV) and
4. Receptors of the immunoglobulin type (ICAM-1and PECAM1)

Selectins- mediate the early tethering and rolling of leukocytes on the vascular endothelium, causing weak attachment of leukocytes to the vessel wall. Integrins- enable firm adhesion of leukocytes to the vascular endothelium. Immunoglobulins- mediate migration of leukocytes from endothelial cells into the surrounding tissues [81].

Migrating poly-morphonuclear leukocytes (PMNs)- also carry adhering platelets to inflammatory extravascular tissue [38].

P-selectin expression

P-selectin is an integral membrane protein located in the alpha-granules of the platelets. [74] It is expressed on the cell surface during cell activation. This protein mediates interactions between platelets, leukocytes and endothelial cells. P-selectin stabilizes initial platelet aggregation[75] and synergizes with platelet activating factor (PAF) and/or RANTES and induce the synthesis of cytokines like interleukin-8 (IL-8) and tumour necrosis factor-alpha (TNF-α) and monocyte chemo attractant protein1 (MCP-1),thus providing localized signals for monocyte adhesion [43].

Soluble P-selectin

The expression of P-selectin is transient, as it is endocytosed [45] or proteolytically shed from the platelet surface into plasma in a biologically active soluble form, while the platelet continues to circulate and function Soluble P-selectin is found to be dependent on the time of sample collection and related to platelet count [46, 47] and it has been proposed to be a reliable marker for *in vivo* platelet activation [48, 49].

P-selectin in plasma may also be partly derived from the endothelium since P selectin is a component of the membrane of the Weibel Palade bodies in these cells

CD40 ligand (CD40L)

CD40L, a member of the TNF-α family is also expressed by platelets [50]. By stimulating the platelets with ADP or thrombin, CD40L is rapidly mobilized from intracellular granules to the platelet surface and trigger an inflammatory response on endothelial cells [50]. CD40L is rapidly cleaved into a soluble form, sCD40L, and shed from the platelet surface in minutes to hours.

Interestingly, GPIIb/IIIa antagonists block the hydrolysis and subsequent release of sCD40L from the platelets. So biological activites of sCD40L can be retained by virtue of sCD40L to bind to GPIIb/IIIa [52]

Platelet-leukocyte aggregates

Platelet-leukocyte aggregates represent an interface between inflammatory, atherogenic and thrombogenic responses. The propensity to form heterotypic aggregates differs between leukocyte subpopulations, with monocytes showing the greatest and lymphocytes the least propensity. PMN and platelet-monocyte interactions mediate targeting of leukocytes to the site of injury and may enhance the synthesis of chemokines and cytokines and adhesion molecules, thus further increasing platelet and leukocyte reactivity [38].

PHYSIOLOGY OF PLATELET SIZE

MPV appears to be a marker, or even a determinant, of platelet function. Large platelets are more reactive than small platelets in vitro. They preferentially and more rapidly aggregate with platelet agonist like ADP, collagen and adrenaline produce more prothrombotic and vasoactive factors including arachidonic acid metabolites (eg. Thromboxane A2), serotonin, β thromboglobulin and ATP. They are associated with a decreased bleeding time (BT; a measure of in vivo haemostatic function).

PLATELET INDICES

Similar to RBC, several indices have been derived from platelets.

The most commonly used are

- Mean Platelet Volume (MPV) and
- Platelet Distribution Width(PDW).

MEAN PLATELET VOLUME (MPV)

Measurement of peripheral blood platelet count tells little about platelet related haemostatic function. However, most haematology analysers, measure another platelet parameter, the mean platelet volume which can give useful clinical and patho-physiological information about patients and vascular diseases.[8]

MEASUREMENT OF PLATELET VOLUME

The optimal method for measuring platelet volume

- electrical impedance (Coulter haematology analyser).
- light diffraction (Technicon).

Alternative and less satisfactory methods includes

- semi-quantitative measurement of diameter on platelet smears.
- flow cytometry[8].

In the Coulter series, cells held in fluid suspension are allowed to flow through a small aperture, which create a change in voltage, proportional to particle size. A raw histogram is generated, and a log-normal curve is fitted to the data. Platelet count is derived from this together with the MPV, which is calculated by numerical integration. Similarly, the Sysmex measures parameters with cells in fluid suspension, in addition, the cells are hydro dynamically focused, ensuring that the cells travel in a straight line through the aperture. This prevents cells flowing through at the edge of the aperture and causing spurious changes in the electrical field. It differs from that of Coulter in that the upper and lower discriminators are both mobile[1]. The distribution curve obtained is thus the actual data and not a fitted curve.

MPV is calculated from the curve by a formula

$$(\text{MPV (fL)} = \text{Pct (\%)} \times 1000 \div \text{Plt } (\times 10^3/\mu\text{L})).$$

In contrast, Technicon instruments uses laser-optic technology to measure the size and granularity of cells in suspension. A beam of light is passed through cells, and the amount of forward scatter is proportional to the size of the particles, whereas side scatter equates to the density or granularity. A platelet histogram is derived from this data, and MPV is calculated as the mode. Differences of up to 40% have been found when Coulter and Technicon results have been compared.[1]

Complete blood count specimens are usually anticoagulated with EDTA that causes platelet to swell in a time dependent manner. Most of the increase in MPV occurs during the first 2 hrs but the process continues over the next 24 hrs. EDTA is thought to increase intracellular cyclic AMP and change plasma membrane permeability[1].

This situation is further complicated since analysers utilising light diffraction measures the particle size by assessing optical density. These analysers record a decreasing MPV with time since platelet swelling results in a lower optical density. As a result, studies using raw MPV measurements made in EDTA are of questionable in clinical or research value unless MPV is assessed at a consistent time following phlebotomy, or once the swelling has ceased at 24 hrs. In contrast MPV measured in high concentration sodium citrate does not change with time[8] and hence considered as the gold standard anticoagulant.

NORMAL VALUES FOR MPV

The normal range for platelet volume has yet to be adequately determined, but studies measuring MPV in sodium citrate in normal subjects suggest a normal range of 4.5 – 8.5 fl with a mean of 6.5 fl[8]. The day to day variation in MPV is small compared with the platelet count.

ROLE OF MEAN PLATELET VOLUME

Some studies have shown that MPV has increased in myocardial infarction, cerebrovascular accident, Alzheimer disease, hypertension and celiac diseases. In contrast it has been shown that MPV decreases in various inflammatory diseases like Rheumatoid arthritis, Ankylosing spondylitis, Ulcerative colitis and acute pancreatitis. It has been suggested that the the dual role of this marker largely depend upon the intensity of inflammation.

Circulating platelets are abundant source of various pro-inflammatory mediators and pro thrombotic factors. Thee play a key role in the initiation and propagation of inflammatory and vascular events. Platelets are anucleate cells and their size mostly depends on the fragmentation of megakaryocytes. Studies have shown that cytokines such as interlukin 3 and interlukin 6 influence megakaryocyte ploidy and can lead to the production of large and reactive platelets. Thus Mean Platelet Volume (MPV) have been proposed as an indirect marker of platelet reactivity.

MATERIALS AND METHODS

STUDY TYPE

Cross - Sectional Study.

STUDY PLACE

This study was done in Department of Medicine, Kilpauk Medical College in association with the Department of Medical Gastroenterology, Microbiology and Pathology, Government Kilpauk hospital, Chennai.

STUDY PERIOD

March 2014 – September 2014.

STUDY POPULATION

During this period 75 cases of cirrhosis with ascitis who are admitted under the Department of Medicine and the patients attending outpatient department, Department of Medical Gastroenterology, Govt. Kilpauk Hospital were examined for Ascitic fluid Infections (AFIs).

INCLUSION CRITERIA

- Age more than 18 years.
- All inpatients and out patients with Decompensated Liver Disease (DCLD), before the first dose of antibiotic administration.

EXCLUSION CRITERIA

- Patients who received antibiotics prior to hospitalization.
- Patients with hollow viscus perforation and secondary bacterial peritonitis.
- Systemic inflammatory diseases.
- Cerebrovascular accident.
- Myocardial infarction.

INFORMED CONSENT

Written informed consent was obtained from each patient. If patients were unable to provide consent, written consent was obtained from their legal guardians (father, mother, spouse, son or daughter). Patients who were unable to provide consent and were not accompanied by a legal guardian were not enrolled in the study.

ETHICAL CONSIDERATION

Ethical with research clearance was obtained from the Ethical Committee Kilpauk Medical College. Written consent done before enrolment.

STATISTICAL DATA

Statistical data obtained with SPSS Software (Statistical Package for Social Sciences) version 20. Univariate analysis was done using Pearson Chi-Square Test and Fisher's Exact Test.

SAMPLE COLLECTION[61]

After history taking and physical examination, all patients proved to have portal hypertension and ascites clinically (i.e., presence of ascites and splenomegaly) and by bedside ultrasonography, who met the above mentioned criteria during the study period, were cordially invited in the study. Consent forms were provided, and the aim of the study was explained. After obtaining written informed consent, patients were enrolled in the study.

MEAN PLATELET VOLUME DETERMINATION

At the time of admission, the skin to be punctured is sterilised with 60% ethanol and allowed to dry. 3ml of blood were drawn and put in the EDTA containing sample bottles.

EDTA blood samples collected at the time of admission were analyzed in automated hematology analysis system. This system measures the platelet size using aperture impedance technology.

All patients samples were processed within 2 hours to avoid bias due to excessive platelet swelling. Previous studies reported that MPV values increase due to platelet swelling when EDTA was used as an anticoagulant. However recent studies have demonstrated that analyzing MPV within 2 hours of sample collection have no effects on platelet size. Reference range of MPV in Kilpauk Medical College is 6-8.5 fl.

For my study I am taking the cut- off value of MPV as 8.5 fl. (as per reference from previous studies)

ERYTHROCYTE SEDIMENDATION RATE

This is the non-specific screening test, that indirectly measures the presence of inflammation in the body. It reflects the tendencies of the RBCs to settle more rapidly in the face of some diseases because of increase in the plasma fibrinogen, immune globulins and acute phase reactants.

METHODS

2ml of venous blood is placed in a tube containing anticoagulant citrate or EDTA of 0.5ml. The anticoagulated blood shouldn't be allowed to stand not more than 2 hours in room temperature. The blood is drawn in the Westergrens

Katz tube upto 200 mark level. The tube is placed in a rack strictly in a vertical position for 1 hour at room temperature, at which time the lowest point of surface meniscus to the upper limit of red cell sediment is measured. The distance of fall of erythrocytes is measured and it is expressed in millimeters in 1 hour.

PARACENTESIS

PREFERRED SITE FOR PARACENTESIS

Left lower quadrant was taken with two finger breadths cephalad and two finger breadths medial to the anterior superior iliac spine *(RUNYON'S SPOT)*[3], where the abdominal wall is thinner with larger pool of fluid. Right lower quadrant was not the choice since appendicectomy scar /dilated caecum are present.

- The Inferior epigastric arteries and midline (collaterals) were escaped.
- Visible collaterals were also escaped.

POSITION OF THE PATIENT

The head end of the bed elevated . Patients with large volume of ascites and thin abdominal wall were "tapped" in this supine position. Patients with less amount of fluid were placed in the lateral decubitus position and tapped from left lower quadrant.

NEEDLE OF CHOICE

Standard metal 1.5 inch, 22 gauge needle is used, obese Individuals with thick abdominal wall use longer needle of 3.5 inch length.

DISINFECTION OF SKIN [6]

As per Universal precautions, gloves that are sterile were worn for the procedure. The skin to be punctured is rubbed using 60% ethanol in a circular fashion approximately 4.5cm in diameter and allowed to air dry. Starting at the center of the circle, 2% povidone iodine was applied, until the entire circle was saturated with iodine and allowed to dry for one minute.

TECHNIQUE OF PARACENTESIS

Under aseptic precautions the disinfected area was injected with local anaesthetic, punctured with 22 gauge needle using "Z tract" technique. The skin was displaced 2cm downward with one gloved hand.

Needle was introduced through the abdominal wall gently. The syringe with the needle was aspirated during insertion. When the needle was released, the skin came back to its ground zero position. This helped the needle pathway to be sealed and post-procedural leak was avoided. About 50 ml of ascitic fluid was withdrawn using syringe.

MACROSCOPIC APPEARANCE

Colour and appearance of the fluid was noted-whether *crystal* clear, transparent or slightly yellow, cloudy yellow, bloody, opaque and chylous, dark brown.

TRANSPORTNG THE SAMPLES

15 ml of fluid each was inoculated into 40 ml of Brain Heart Infusion (BHI) broth and 40 ml of Thioglycollate broth at the bedside respectively. The BHI and the thioglycollate broth bottles were immediately transported to the laboratory and incubated at 36°c. Another 4ml was collected in a sterile screw capped test tube and sent to the microbiology laboratory .

PROCESSING SAMPLES

When the test tube was received in the microbiology laboratory, conventionally, centrifugation speed was 3000 revolutions/10 minutes and centrifuged sample was inoculated into BHI broth in the laboratory, followed up and processed along with the BHI broths inoculated at the bedside[15].

MICROSCOPIC EXAMINATION

From the sediment direct gram stain, acid fast stain was performed.

BACTERIAL CULTURE

A part of the sediment was lysed *with Triton X*-at room temperature, kept 5 minutes and inoculated into Blood agar, Mac Conkey agar incubated aerobically at 37 °c for 48 hrs, Chocolate agar which incubated at 37 °c in 5% CO2 for 48 hrs, Brain heart infusion agar was incubated for 48 hrs. The broth bottles were followed for 7 days with aerobic and anaerobic subculturing at 24, 48 and 168 hrs. Additionally, subculture from bedside BHI broth onto 2% Tween 80 BAP was done[11].

CONVENTIONAL BHI VS BEDSIDE BHI

IDENTIFYING ISOLATES

The preliminary tests-motility, catalase, oxidase Gram stain, were performed on all isolates and based on the results further identification of the isolates were done by standard microbiological tests.

ANTIMICROBIAL SUSCEPTIBILITY

The Isolates subjected to antimicrobial susceptibility testing by Kirby-Bauer disc diffusion method.

Mueller-Hinton agar (MHA) plate is inoculated with 0.5 McFarland standard of the isolate to get a lawn culture. Using sterile forceps, the antibiotic discs were placed over the agar surface, incubated at 37°C in

ambient air for 16 to 18 hrs. The results were interpreted as per Clinical Laboratory Standards Institute Guidelines (CLSI Guidelines 2012).

The Escherichia coli ATCC 25922, Staphylococcus aureus ATCC 25923 and Pseudomonas aeruginosa ATCC 27853 were used as quality control strains.

YELLOW PIGMENTED PSEUDOMONAS

ASCITIC FLUID - CELL COUNT

About 4 ml of ascitic fluid was placed in a tube containing the anticoagulant EDTA (ethylenediaminetetraacetic acid) for cell count. Cell count is analysed by manual method.

ASCITIC FLUID-BIOCHEMISTRY

About 5 ml of ascitic fluid was placed in a tube and sent for biochemistry to estimate Glucose, Total protein, albumin (routine), amylase and lactate dehyrogenase (in clinically relevant cases).

OBSERVATION AND RESULTS

Ascitic fluid was tapped from 75 Decompensated Liver Disease (DCLD) patients (44 Out patients and 31 In patients) under aseptic precautions.

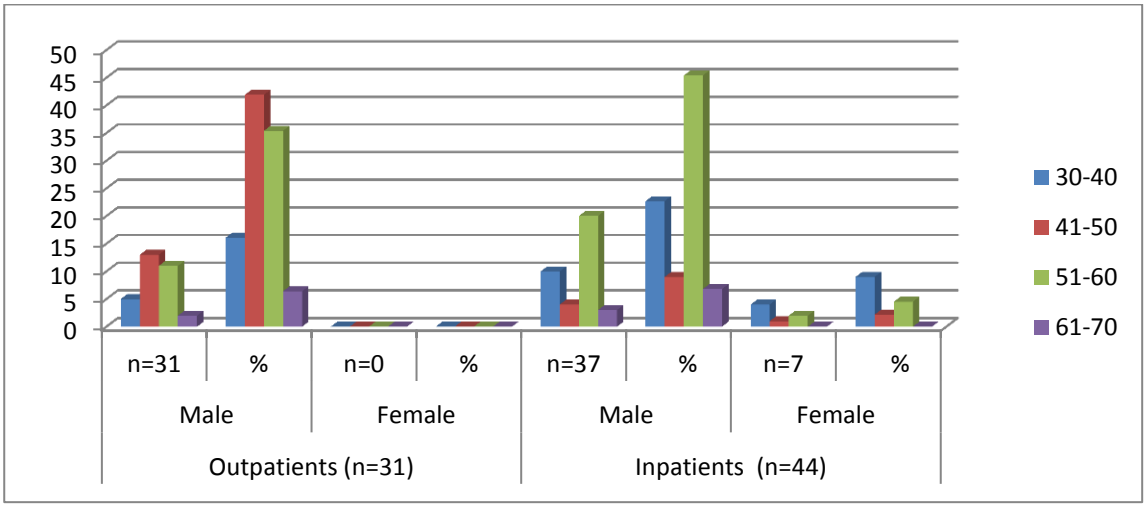
CBC, ESR, LFT, RFT, Ascitic fluid PMN count ,were performed in all the patients.

Bacterial culture is done for the ascitic fluid samples and the isolates are identified by standard microbiological tests. Antimicrobial susceptibility testing is done for the significant isolates according to CLSI Guidelines 2012.

Univariate analysis of the data was done by Pearson Chi-Square Test and Fisher's Exact Test. The p values less than 0.01 were considered as highly stastiscally significant ($p < 0.01$).The p values less than 0.05 were considered as stastistically significant ($p < 0.05$) and Study results are presented as follows

TABLE 1: DISTRIBUTION OF AGE IN DCLD PATIENT (n=75)

Age in Years	Outpatients (n=31)				Inpatients (n=44)			
	Male		Female		Male		Female	
	n=31	%	n=0	%	n=37	%	n=7	%
30-40	5	16.1	0	0	10	22.7	4	9
41-50	13	41.9	0	0	4	9	1	2.2
51-60	11	35.4	0	0	20	45.4	2	4.5
61-70	2	6.4	0	0	3	6.8	0	0



Most of the DCLD out patients are in the age group of 41-50yrs, and among the in patients, most of them are in the age group of 51-60 yrs. The mean age of all the patients was 49.52 yrs. The mean age among out patient was 49.03 years. The Median age was 50 years. Mean age among inpatients was 49.86 years. Many of them are males.

TABLE 2: ETIOLOGY AND SEX DISTRIBUTION PATTERN OF DCLD PATIENTS: (n=75)

ETIOLOGY	Out patients (31)				Inpatients (44)			
	MALE		FEMALE		MALE		FEMALE	
	n=31	%	n=0	%	n=37	%	n=7	%
Alcohol	24	77.4	0	0	29	65.9	1	2.3
HBV	3	9.6	0	0	2	4.5	6	13.6
HCV	0	0	0	0	1	2.3	0	0
Alcohol+HBV	2	6.4	0	0	1	2.3	0	0
Alcohol+HCV	1	3.2	0	0	0	0	0	0
OTHERS	1	3.2	0	0	4	9	0	0

Alcoholic Liver cirrhosis is the frequent cause of ascites among men in outpatient (77.4%) and inpatient (65.9%) category.

HBV related cirrhosis is the most common cause among the inpatient females(85.7%).

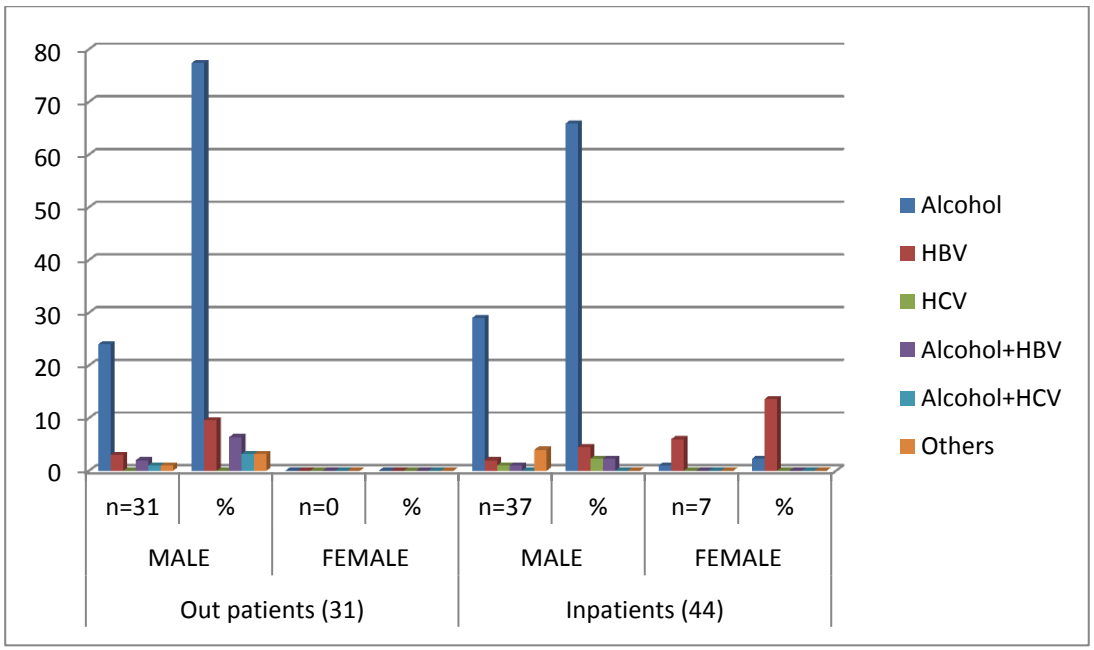
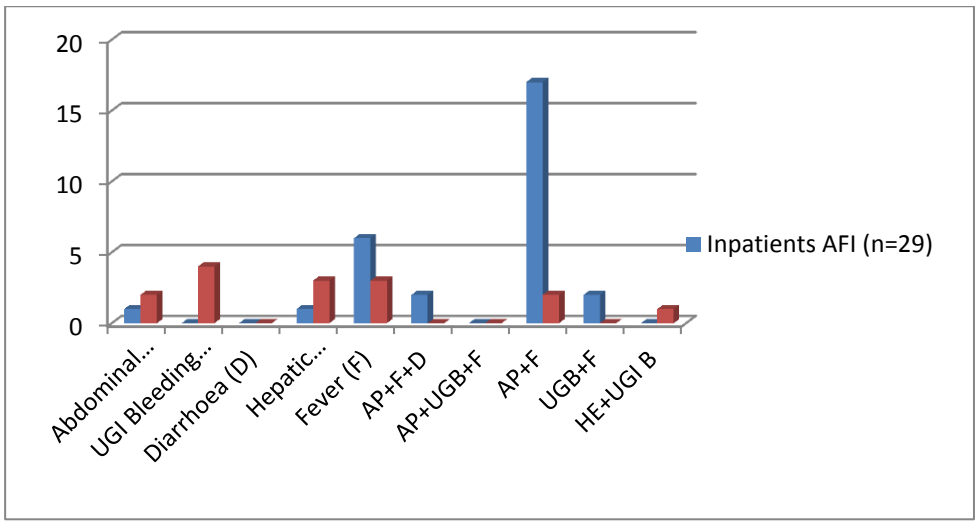


TABLE 3: SIGNIFICANT CLINICAL FEATURES IN CIRRHOTIC INPATIENTS PRESENTING WITH OR WITHOUT AFI

SIGNS & SYMPTOMS	Inpatients n=44	
	AFI (n=29)	NO AFIs (n=15)
Abdominal Pain(AP)	1	2
UGI Bleeding (UGB)	0	4
Diarrhoea (D)	0	0
Hepatic Encephalopathy (HE)	1	3
Fever (F)	6	3
AP+F+D	2	0
AP+UGB+F	0	0
AP+F	17	2
UGB+F	2	0
HE+UGI B	0	1

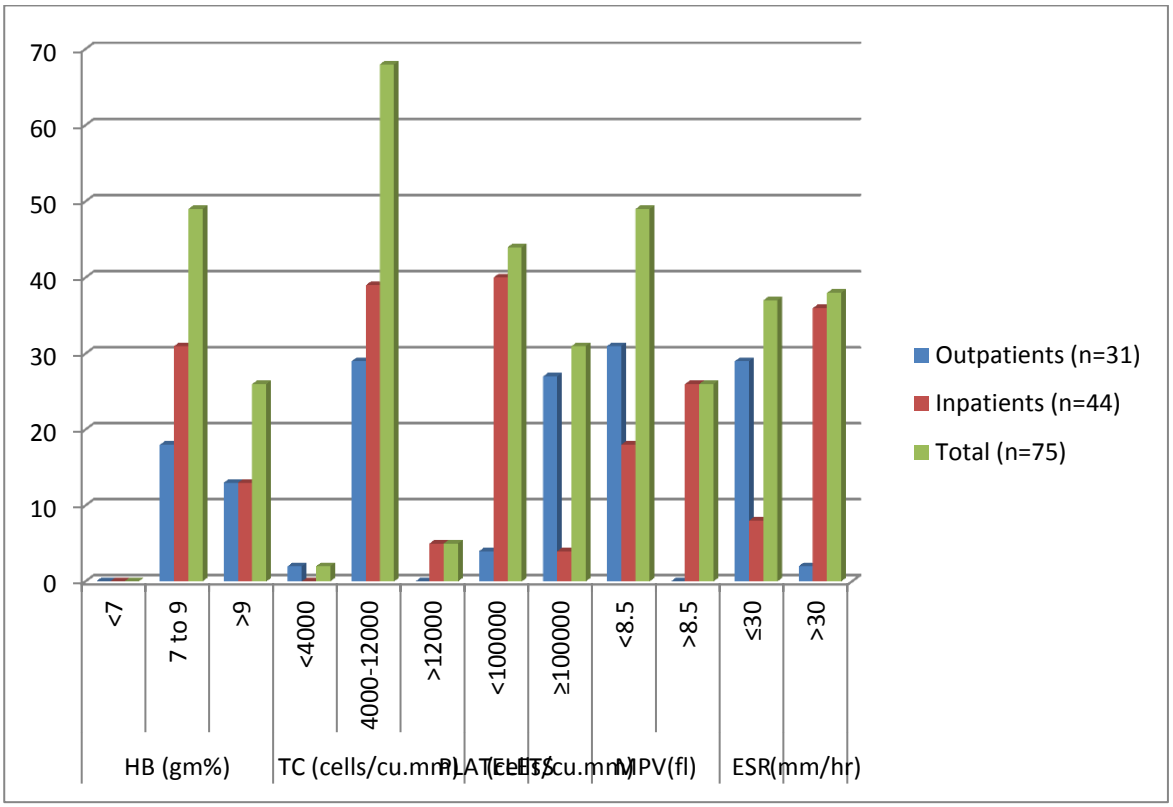


Among the patients with ascitic fluid infections, the most common presenting symptoms are a combination of Abdominal pain and fever 17 out of 29 (58.6%) whereas fever alone is present in 6 out of 29 patients(20.6%). Abdominal pain alone is present in 1 out of 29 patients(3.4%).

TABLE 4: LABORATORY PARAMETERS IN CIRRHOTIC PATIENTS: (n=75)

Laboratory Parameters		**Outpatients (n=31)**	**Inpatients (n=44)**	**Total (n=75)**
HB (gm%)	<7	0	0	0
	7-9	18	31	49
	>9	13	13	26
TC (cells/cu.mm)	<4000	2	0	2
	4000-12000	29	39	68
	>12000	0	5	5
PLATELETS (cells/cu.mm)	<100000	4	40	44
	≥100000	27	4	31
MPV(fl)	<8.5	31	18	49
	>8.5	0	26	26
ESR	≤30	29	8	37
(mm/hr)	>30	2	36	38

By comparing the laboratory parameters among inpatient and outpatients, it is found from the above table that Total Leucocyte Count (TC) >12000 was found in 5 out of 44 (11.36%) of patients, whereas 0 out of 44 none of the out patients had elevated TC above>12000.



Platelet count is reduced to less than 100000 in 40 out of 44 (91%) among the inpatients. MPV was significantly elevated to more than 8.5 fl in 26 out of 44 (59%) inpatients. In outpatient none of them had an elevated MPV. ESR elevated to more than 30 in 36 out of 44 (81.8%) inpatients. Only 2 out of 31(6.4%) outpatients had elevated ESR to more than 30.

TC, Platelet count, MPV and ESR were found to be statistically significant among inpatients and outpatients.

TABLE 5 : LABORATORY PARAMETERS IN CIRRHOTIC PATIENTS WITH OR WIHOUT AFI

Laboratory Parameters		AFI (n=29)	WIHOUT AFI (n=15)	Total (n=44)
HB (gm%)	<7	1	2	3
	7-9	18	10	28
	>9	10	3	13
TC (cells/cu.mm)	<4000	0	0	0
	4000-12000	24	15	39
	>12000	5	0	5
PLATELETS (cells/cu.mm)	<100000	27	13	40
	≥100000	2	2	4
MPV (fl)	<8.5	5	13	18
	>8.5	24	2	26
ESR (mm/hr)	≤30	1	7	8
	>30	28	8	36

The above table compare the laboratory parameters among the patients with or without Ascitic fluid infection and found that TC was elevated to more than 12000 in 5 out of 29 patients(17.2%) with AFI and no patient without AFI had elevated count.

Platelet count was reduced to 100000 in 27 out of 29 patients (93%) with AFI and in 13 out of 15 (86%) patients without AFI

MPV was elevated to more than 8.5 in 24 out of 29 (83%)patients with AFI and in 2 out of 15 (13.3%) of patients without AFI.

ESR was elevated to more than 30 in 28 out of 29 (96%) of patients with AFI and in 8 out of 15 (53%) patients without AFI. So, TC, MPV and ESR were statistically significant among the patients with and without AFI

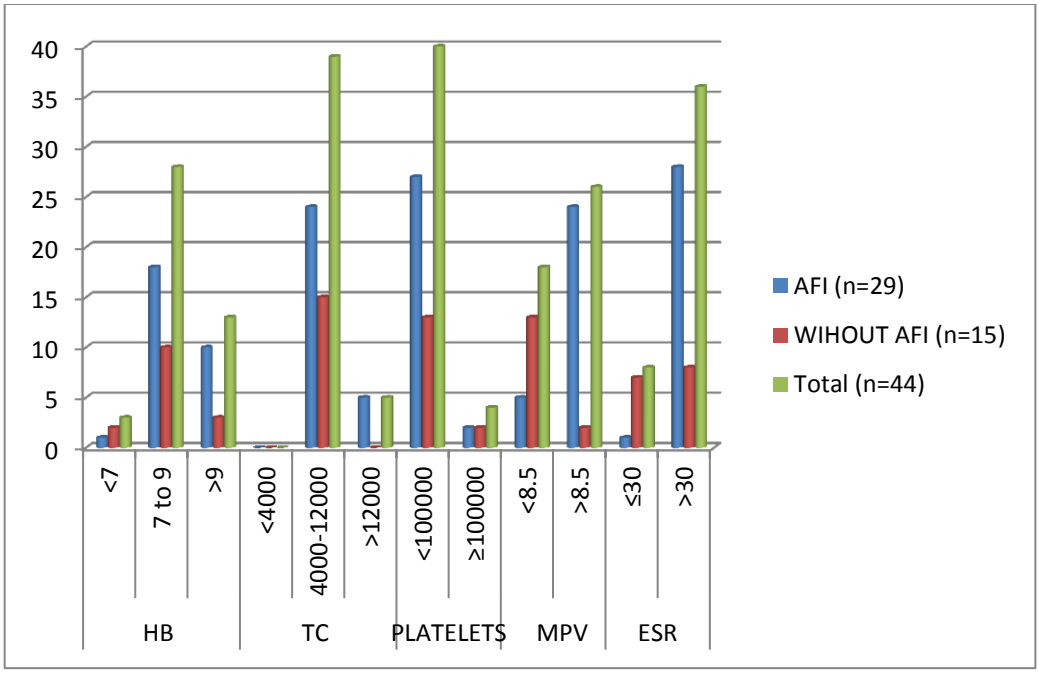


TABLE 6: LABORATORY PARAMETERS LFT IN CIRRHOTIC PATIENTS (n=75)

Laboratory Parameters		Outpatients (n=31)	Inpatients (n=44)	Total (n=75)
S.BILIRUBIN (mg%)	<3	13	0	13
	>3	18	44	62
TOTAL PROTEIN(gm/dl)	<6.5	19	44	63
	>6.5	12	0	12
S.ALBUMIN (gm%)	<3.5	12	39	51
	≥3.5	19	5	24
AST(U/L)	<30	10	1	11
	>30	21	43	64
ALT(U/L)	<30	24	2	26
	>30	7	42	49
PT-INR	≤1.5	25	25	50
	>1.5	6	19	25

The above table compares the parameters of Liver Function Test among the inpatient and outpatients, and it is found that Serum Bilirubin was elevated to more than 3mg% in 18 out of 31 (58%) outpatient, whereas it is elevated to more than 3 in all inpatients 44 out of 44 (100%).

Total protein was reduced to less than 6.5gm% in 19 out of 31 (61.2%) outpatient, whereas all inpatients had reduced Total Protein 44 out of 44 (100%). S albumin reduced to 3.5gm% in 39 out of 44 (88.8%) in inpatients & outpatients 12/31 (38.7%)

AST, ALT and PT-INR had no statistically significant correlation from the above table.

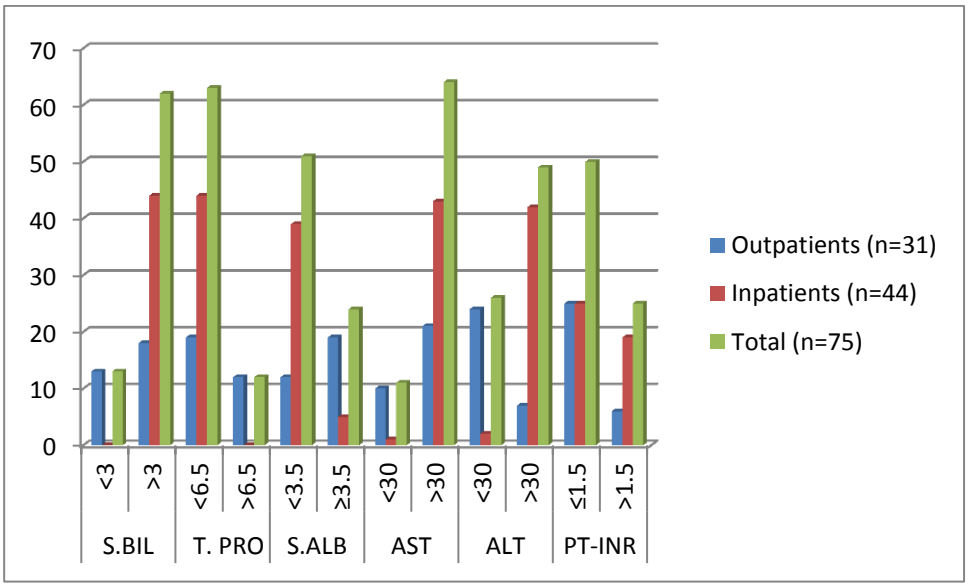


TABLE 7: LABORATORY PARAMETERS LFT IN IN PATIENTS WITH OR WITHOUT AFI

Laboratory Parameters		AFI (n=29)	WITHOUT AFI (n=15)	Total (n=75)
S.BILIRUBIN (mg%)	<3	0	0	0
	>3	29	15	44
TOTAL PROTEIN(gm/dl)	<6.5	29	15	44
	>6.5	0	0	0
S.ALBUMIN (gm%)	<3.5	25	14	39
	≥3.5	4	1	5
ALT(U/L)	<30	2	0	2
	>30	27	15	42
AST(U/L)	<30	1	0	1
	>30	28	15	43
PT-INR	≤1.5	17	8	25
	>1.5	12	7	19

The above table compares the parameters of Liver Function Test among the patients with AFI and without AFI, and it is found that Serum Bilirubin was elevated to more than 3 in all patients with AFI 29 out of 29 (100%) and without AFI 15 out of 15 (100%). Total protein was reduced to less than 6.5gm% in all patients with AFI 29 out of 29 (100%).

Serum albumin was reduced to less than 3.5gm% in 25 out of 29 (86.2%) in patients with AFI and in 14 out of 15 (93.3%) in patients without AFI. AST, ALT and PT-INR had no statistically significant correlation from the above table.

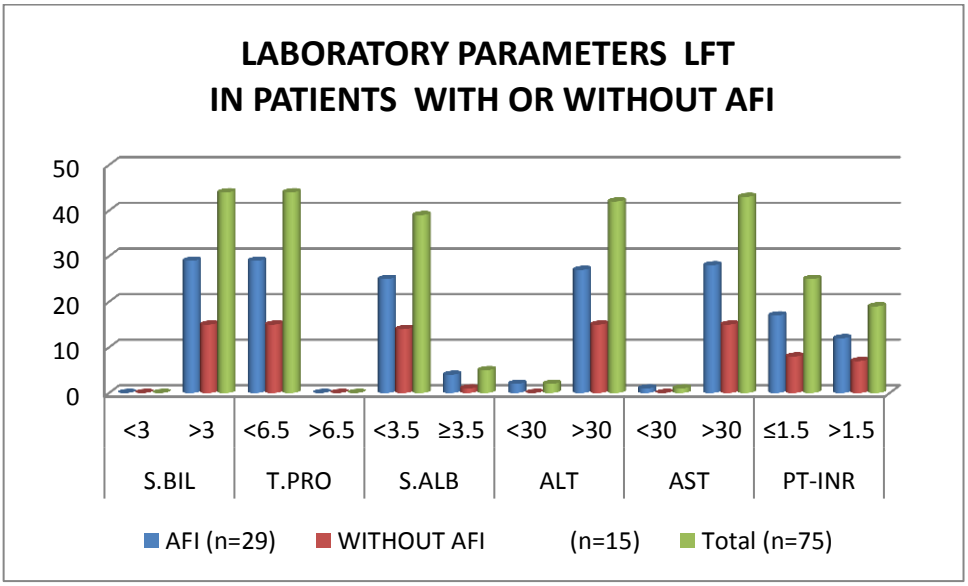
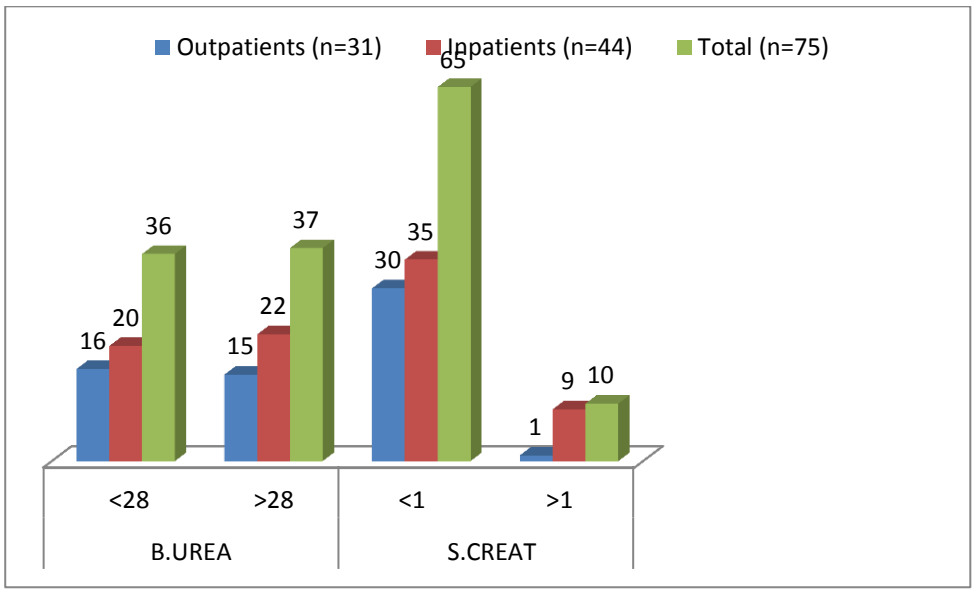


TABLE 8: LABORATORY PARAMETERS RFT IN CIRRHOTIC PATIENTS (n=75)

Laboratory Parameters		Out patients (n=31)	In patients (n=44)	Total (n=75)
B.UREA (mg%)	<28	6	20	36
	>28	15	22	37
S.CREATININE (mg%)	<1	30	35	65
	>1	1	9	10

The above table compares the parameters of Renal Function Test among the inpatient and outpatients, and it is found that Blood Urea was elevated to more than 28mg% in 15 out of 31 (48.3%) outpatient and in 22 out of 44(50%) inpatient. Serum creatinine was elevated to more than 1 mg% in 1 out of 31 (3.2%) outpatient and in 9 out of 44 (20.4%) inpatient.

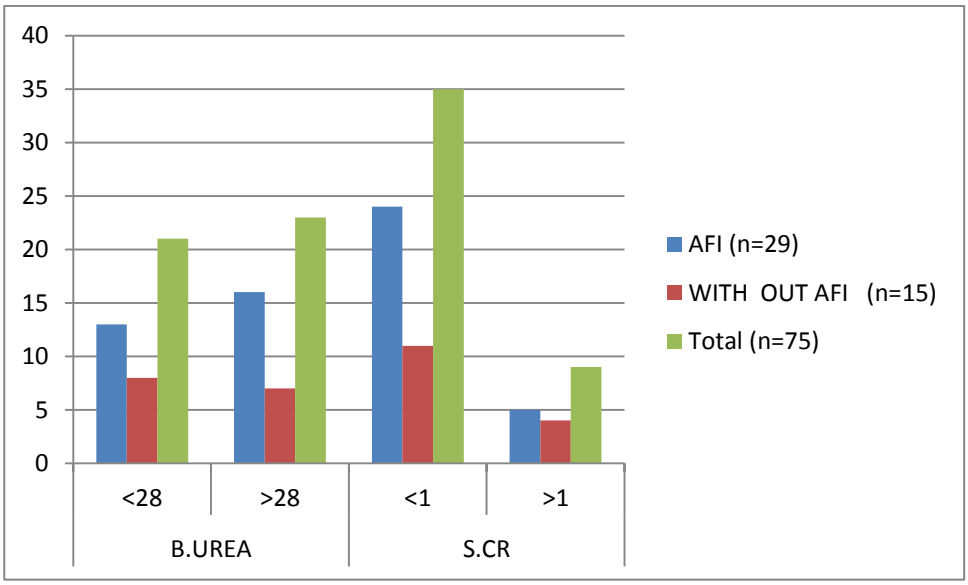


So, Blood urea and serum creatinine had no statistically significant correlation among inpatient and outpatient.

TABLE 9: LABORATORY PARAMETERS RFT IN IN PATIENTS WITH OR WITHOUT AFI

Laboratory Parameters		AFI (n=29)	WITHOUT AFI (n=15)	Total (n=75)
B.UREA (mg%)	<28	13	8	21
	>28	16	7	23
S.CR (gm%)	<1	24	11	35
	>1	5	4	9

The above table compares the parameters of Renal Function Test among the patients with AFI and without AFI, and it is found that Blood Urea was elevated to more than 28mg% in 16 out of 29 (55.1%) patient with AFI and in 7 out of 15 (46.6%) patient without AFI. Serum creatinine was elevated to more than 1 mg% in 5 out of 29 (17.2%) patient with AFI and in 4 out of 15 (26.6%) patient wihout AFI



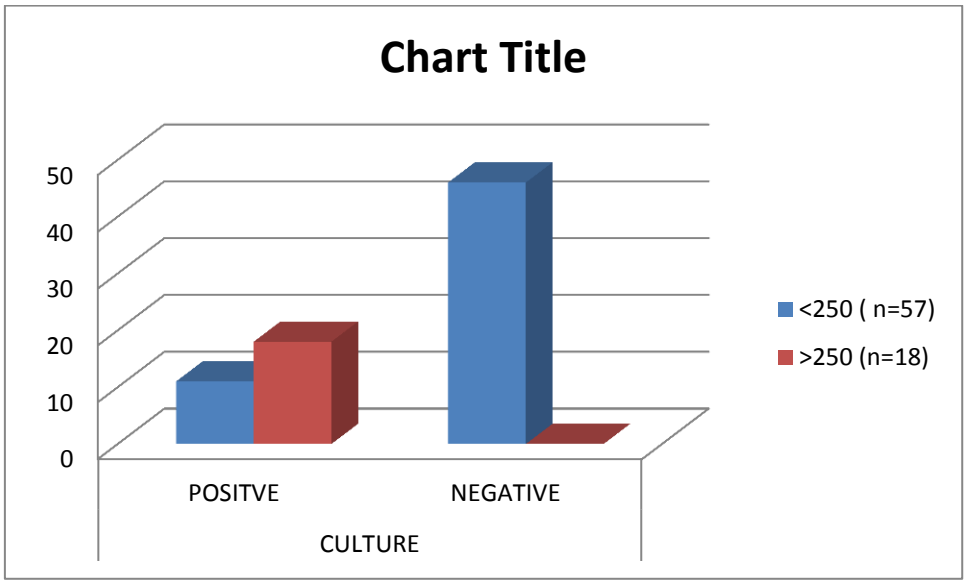
So, Blood urea and serum creatinine had no statistically significant correlation among the patients wih or without AFI.

TABLE 10: COMPARISION BETWEEN ASCITIC FLUID PMN COUNT AND CULTURE

PMN COUNT (cells/cu.mm)	CULTURE	
	POSITVE	NEGATIVE
<250 (n=57)	11	46
>250 (n=18)	18	0

In the ascitic fluid analysis, 57 patient had Poly Morpho Neutrophil count less than 250. Out of 57 patients, 11 patients had positive ascitic fluid culture report.

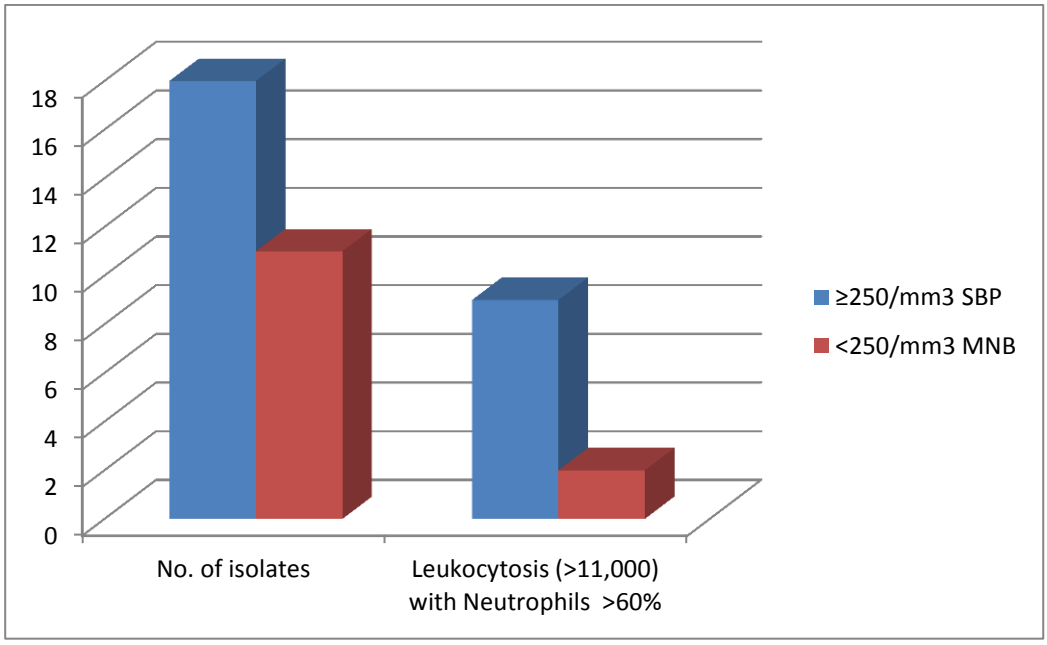
18 patients had Poly Morpho Neutrophil count more than 250. All the patient having PMN count more than 250 had positive ascitic fluid culture positivity.



- Spontaneous Bacterial Peritonitis (SBP) =18
- Monomicrobial Nonneutrocytic Bacterascites (MNB) =11

TABLE 11 : COMPARISON OF BLOOD NEUTROPHIL COUNT VS ASCITIC FLUID IN PATIENTS WITH AFIS:

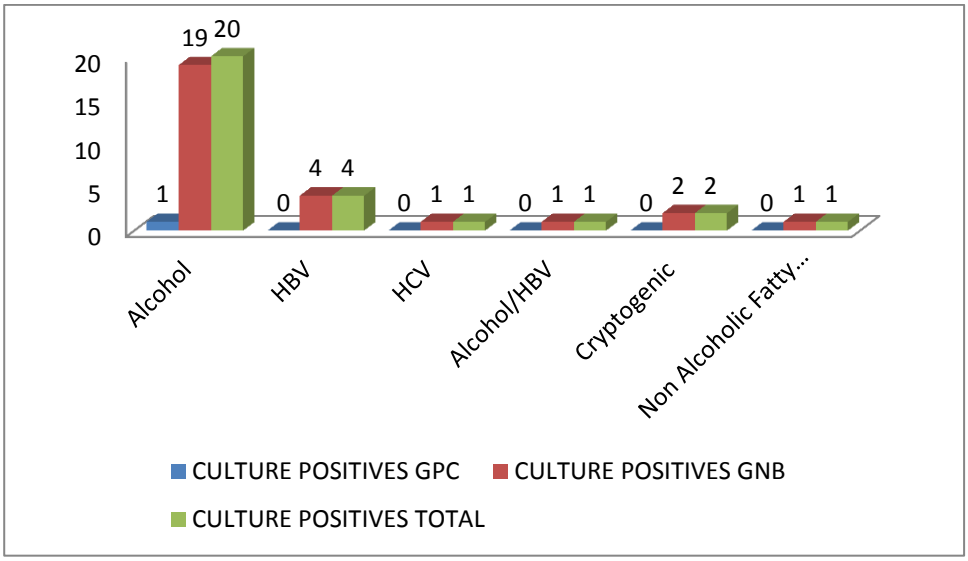
Ascitic fluid PMN count	AFIs	No. of isolates	Leukocytosis (>11,000) with Neutrophils >60%
≥250/mm^3	SBP	18	9
<250/mm^3	MNB	11	2



From the above table it is inferred that, out of 18 patients having SBP, 9 had leucocyte count more than 11000 with neutrophils more than 60% Out of 11 patients having MNB, 2 had leucocyte count more than 11000 with neutrophils more than 60.

TABLE 12: ASCITIC FLUID INFECTIONS (AFIS) IN CIRRHOTICS OF VARIED ETIOLOGIES.

ETIOLOGICAL FACTORS	CULTURE POSITIVES		
	GPC n=1	GNB n=28	TOTAL n=29
Alcohol	1	19	20
HBV	0	4	4
HCV	0	1	1
Alcohol/HBV	0	1	1
Cryptogenic	0	2	2
Non Alcoholic Fatty Liver Disease	0	1	1



The above table shows that, the most common organism causing ascitic fluid infection was gram negative bacilli 28 out of 29 (96.5%). Alcohol is the most common risk factor for ascitic fluid infection 20 out of 29 (68.9%)

TABLE 13: MICROBIAL PROFILE ISOLATED AMONG INPATIENTS WITH DCLD

PATIENT CATEGORY		CULTURE POSITIVES	GPC	GNB
INPATIENTS (44)	Males(37)	26	1	25
	Females(7)	3	0	3
TOTAL		**29**	**1**	**28**

The above table shows that, among the inpatient 37 male, 26 patient had AFI. Out of 26 patient, 25 patient had ascitic fluid infection caused by gram negative bacilli (96.1%) Out of 7 female inpatient, 3 had ascitic fluid infection. All of them were infected by gram negative bacilli (100%)

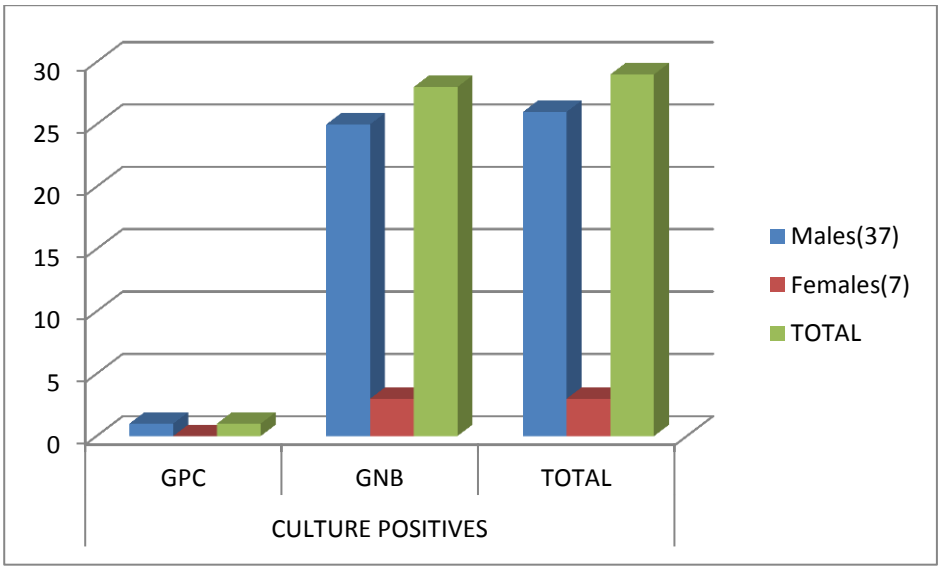


TABLE 14: CLASSIFICATION OF ASCITIC FLUID INFECTIONS IN CIRRHOTICS PATIENTS VARIANTS OF AFIs

VARIANTS	TOTAL	Culture Positives	
		GPC	GNB
Spontaneous bacterial peritonitis (SBP)	18	0	18
Monomicrobial non-neutrocytic bacterascites	11	1	10
TOTAL	**29**	**1**	**28**

Among the asctic fluid infection in DCLD patients, 18 out of 29(62%) had SBP. 11out of 29(37.9%) had MNB. The most common organism was gram negative bacilli in both SBP and MNB category.

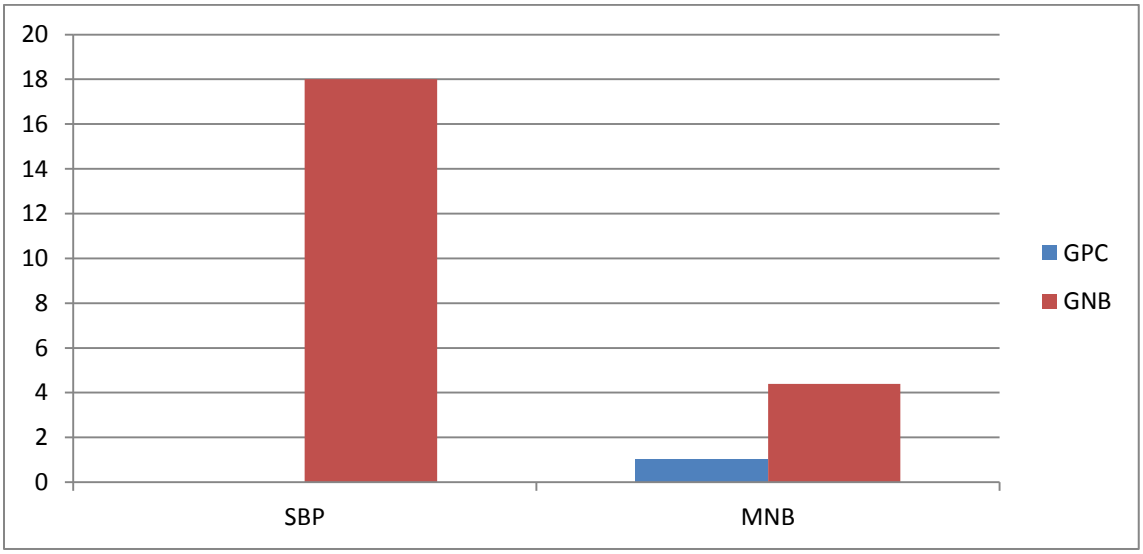


TABLE:15 RELATIONSHIP BETWEEN MPV AND VRIOUS ETIOLOGIES OF CIRRHOSIS

ETIOLOGY		MPV		TOTAL	P VALUE
		<8.5	**>8.5**		
ALCOHOL	YES	39	19	58	0.927
	NO	10	7	17	
HBV	YES	9	5	14	0.522
	NO	40	21	61	
HCV	YES	2	0	2	0.296
	NO	47	26	73	

From the above table it was inferred that MPV had no statistically significant correlation with various etiologies of Decompensated Liver Disease.

TABLE 16: RELATIONSHIP BETWEEN MPV AND VARIOUS CLINICAL FEATURES

CLINICAL FEATURES		MPV		TOTAL	P VALUE
		<8.5	>8.5		
Abdominal pain	Yes	4	20	24	0.000
	no	45	6	51	
Fever	Yes	7	25	32	0.000
	No	42	1	43	
UGI bleed	Yes	6	1	7	0.234
	No	43	25	68	
HE	Yes	5	0	5	0.092
	No	44	26	70	
Diarrhea	Yes	0	2	2	0.049
	No	49	24	73	

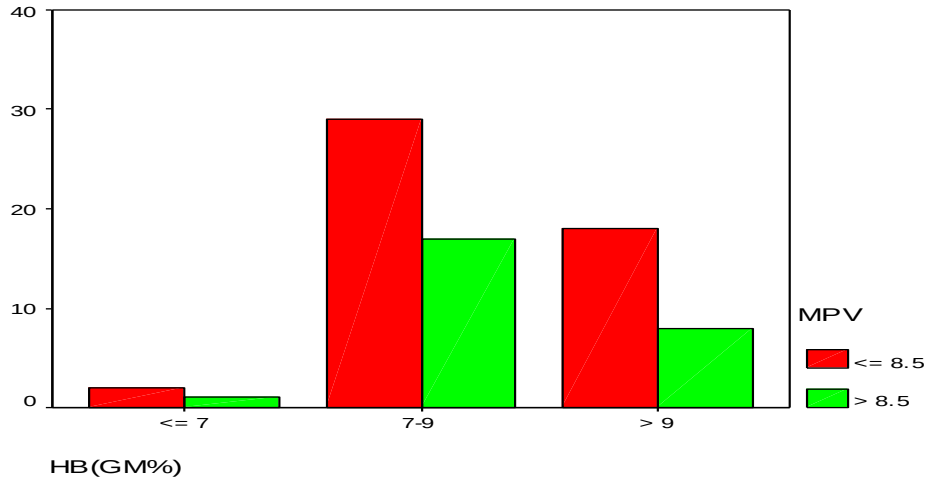
The above table shows that MPV was elevated in 20 out of 24 (83.3%) patients having abdominal pain with a significant p value of less than 0.005.

MPV was elevated in 25 out of 32 (78.1%) patients having fever with a significant p value of less than 0.005.

MPV had no statistical significance with UGI bleed, Hepatic Encephalopathy and diarrhea.

TABLE 17: RELATIONSHIP BETWEEN MPV AND HAEMOGLOBIN

LAB.VALUES		MPV (fl)		TOTAL n=75	P VALUE
		<8.5 n=59	>8.5 n=26		
Hb(gm%)	<7	2	1	3	0.868
	7-9	29	17	46	
	>9	18	8	26	



- Out of 75 patients, 46 patients had haemoglobin value between 7 and 10.
- 3 out of 75 had HB less than 7.
- 26 out of 75 had HB more than 7.
- MPV had no statistically significant correlation with Haemoglobin.

TABLE 18: RELATIONSHIP BETWEEN MPV AND TOTAL COUNT

LAB.VALUES		MPV (fl)		TOTAL n=75	P VALUE
		<8.5 n=59	>8.5 n=26		
TC (cells/cu. mm)	<4000	4	0	4	0.001
	4000-12000	45	21	66	
	>12000	0	5	5	

The above table compares the MPV with Total Leucocyte count.

- Out of 75 patients, 66(88%) had TC between 4000-12000. Out of 66 patients, 21 had MPV >8.5(31.8%)
- 5 out of 75 patients had had TC more than 12000(6.6%). All 5 patients had MPV >8.5(100%)
- MPV had statistically significant correlation with total Leucocyte count with a P value <0.005

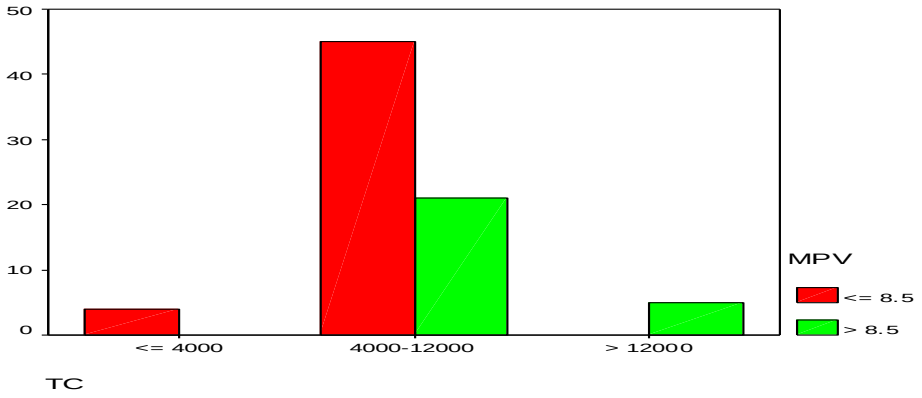


TABLE 19: RELATIONSHIP BETWEEN MPV AND ESR

LAB.VALUES		MPV (fl)		TOTAL n=75	P VALUE
		<8.5 n=59	>8.5 n=26		
ESR (mm/hr)	<=30	37	0	37	0.001
	>30	12	26	38	

The above table compares the MPV with Erythrocyte Sedimentation Rate.

- Out of 75 patients, 37(49.3%) had ESR less than 30. Out of 37 patients, none had MPV >8.5(0%)
- 38 out of 75 patients had ESR more than 30 (50.6%). Out of 38 patients, 26 had MPV >8.5(68.4%)
- MPV had statistically significant correlation with Erythrocyte Sedimentation Rate with a P value <0.005

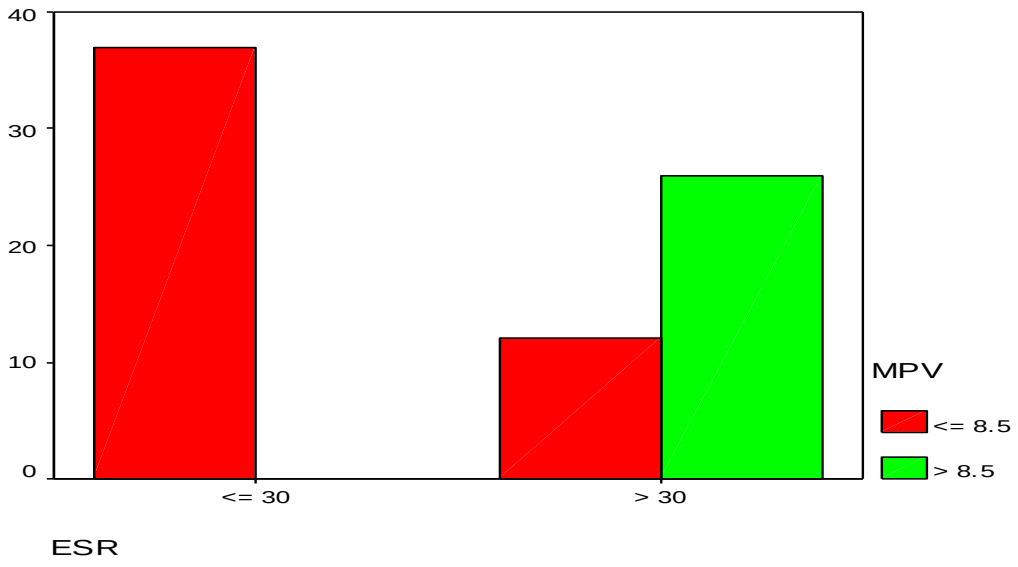


TABLE 20 : RELATIONSHIP BETWEEN MPV AND PLATELETS

LAB.VALUES		MPV (fl)		TOTAL n=75	P VALUE
		<8.5 n=59	>8.5 n=26		
platelets (cell/cu.mm)	<=100000	20	24	44	0.000
	>100000	29	2	31	

The above table compares the MPV with Platelet count.

- Out of 75 patients, 44(58.6%) had platelet count <100000.Out of 44 patients, 20 had MPV <8.5(45.4%)
- 24 out of 44 patients with platelet count <100000 had MPV >8.5(54.5%) whereas 2 out of 31 patients with platelet count <100000 had MPV >8.5(6.4%)
- MPV had statistically significant correlation with Platelet count with a P value <0.005

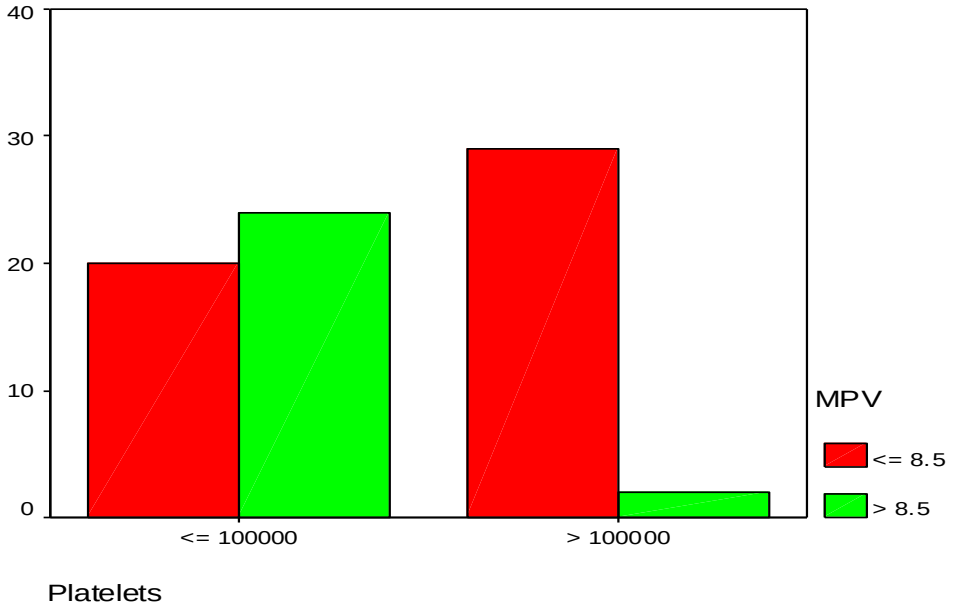


TABLE 21: RELATIONSHIP BETWEEN LFT/ RFT AND MPV

LAB VALUES		MPV		Total	PVALUE
		<8.5	>8.5		
S.Bilirubin	<3	13	0	13	0.002
	>3	36	26	62	
TOTAL		59	26	75	
S.Albumin	<3.5	19	19	38	0.005
	>3.5	30	7	37	
TOTAL		59	26	75	
S.Creatinine	<1	43	22	65	0.479
	>1	6	4	10	
TOTAL		59	26	75	

The above table compares the MPV with S.Bilirubin, S.Albumin and S.Creatinine.

- Out of 62 patients with S.Bilirubin >3mg%, 26 patients had MPV >8.5(41.9%). None with S.Bilirubin < 3mg% had MPV >8.5(0%)
- Out of 38 patients with S.Albumin <3.5mg%, 19 patients had MPV >8.5(50%).
- Out of 10 patients with S.Creatinine >1mg%, 4 patients had MPV >8.5(40%).
- MPV had no statistically significant correlation with S.Bilirubin, S.Albumin, S.Creatinine

TABLE 22: RELATIONSHIP BETWEEN MPV AND PMN COUNT

LAB.VALUES		MPV (fl)		TOTAL n=75	P VALUE
		<8.5 n=59	>8.5 n=26		
PMN (cell/cu.mm)	<250	48	12	60	0.000
	>250	1	14	15	

- Out of 60 patients with PMN count <250, 12 had MPV>8.5(20%)
- Out of 15 patients with PMN count >250, 14 had MPV>8.5(93.3%)

So, MPV was significantly correlated to PMN>250 with a P value of 0.000.

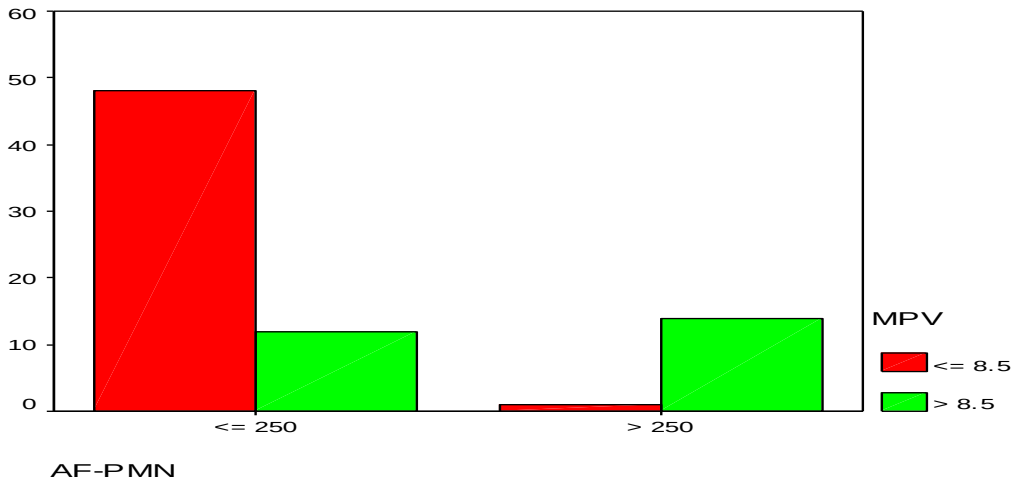


TABLE 23: RELATIONSHIP BETWEEN MPV AND CELL CULTURE

LAB.VALUES		MPV (fl)		TOTAL n=75	P VALUE
		<8.5 n=59	>8.5 n=26		
Cell culture	Growth	5	24	29	0.000
	No growth	44	2	46	

Out of 29 positive ascitic fluid culture, 24 patients had elevated MPV of more than 8.5(82.7%) Whereas only 2 out of 46 patients with ascitic fluid culture had elevated MPV of more than 8.5(4.3%)

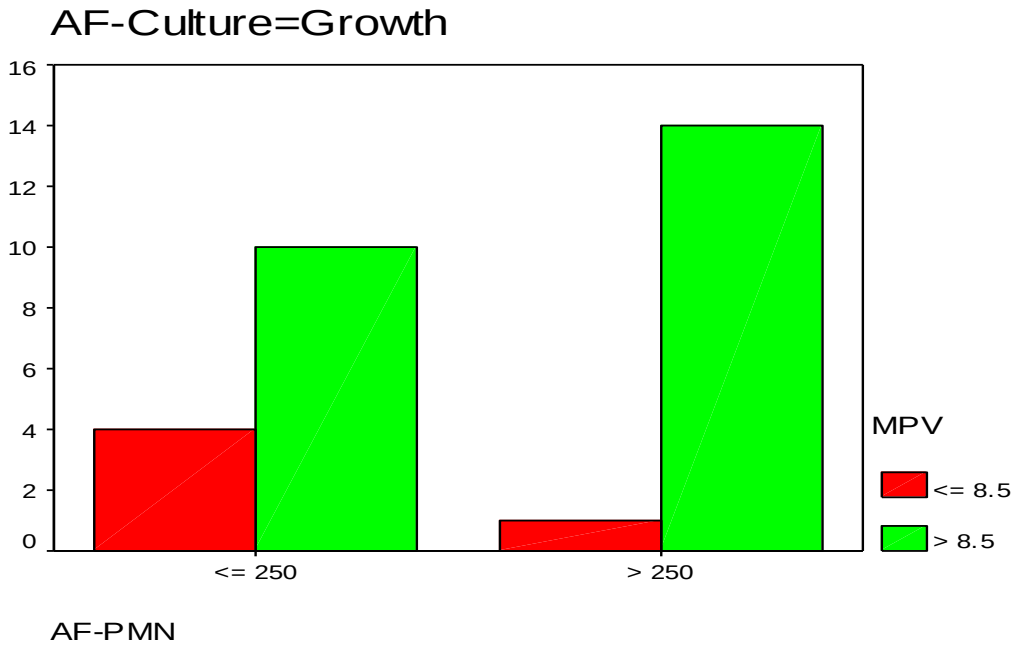
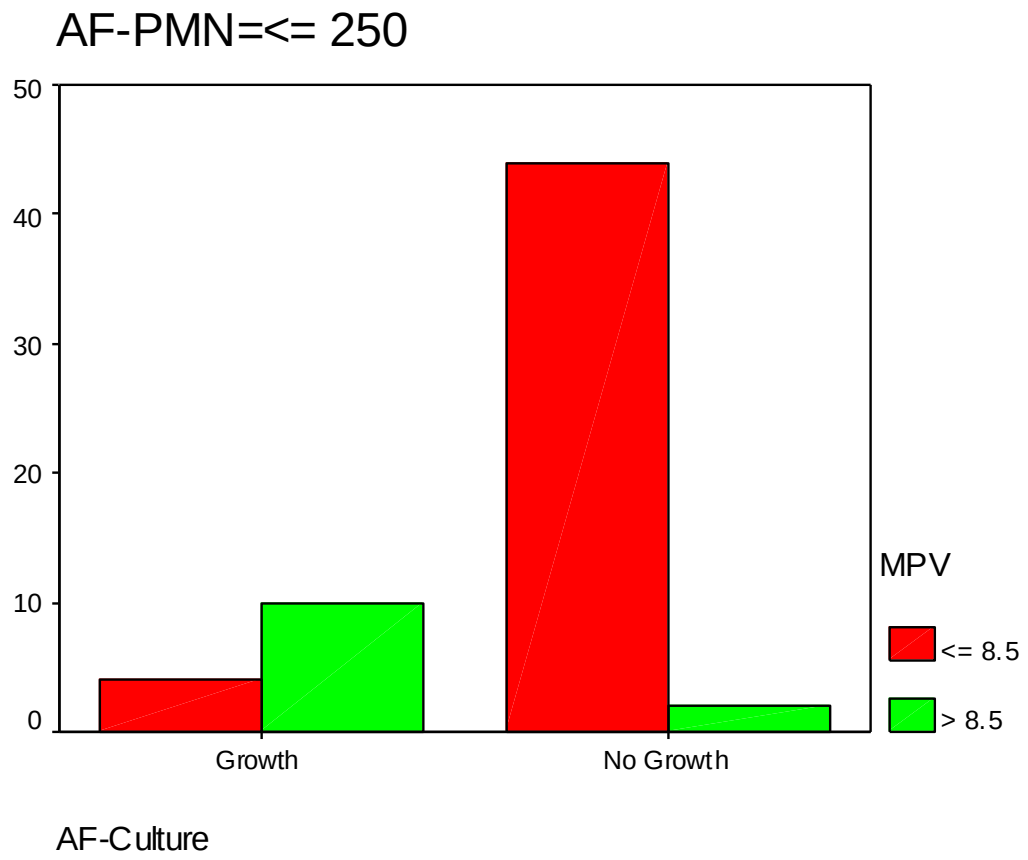


TABLE 24: RELATIONSHIP BETWEEN PMN / CELL CULTURE AND MPV

PMN	Culture	MPV		Total	P VALUE
		<8.5	>8.5		
<250	Growth	4	10	14	0.000
	No Growth	44	2	46	
TOTAL		48	12	60	
>250	Growth	1	14	15	
	No Growth	0	0	0	
TOTAL		1	14	15	

The above table shows that, 15 patients had both features of PMN count>250 cells/cu.mm and positive ascitic fluid culture.

- Out of these 15 patients, 14 had MPV more than 8.5(93.3%). 14 patients had both features of PMN count<250 cells/cu.mm and positive ascitic fluid culture.
- Out of these 14 patients, 10 had MPV more than 8.5(71.4%).



So, MPV had significant correlation with both PMN count and Ascitic fluid culture.

DISCUSSION

The present study entitiled *"MEAN PLATELET VOLUME AN INDICATOR OF ASCITIC FLUID INFECTION IN CIRRHOTIC PATIENTS"* done in Government Kilpauk Medical college and hospital was a cross sectional study. This study was done in patients attending the outpatient Department and in inpatients with DCLD and its complications from March 2014 to September 2014.

Ascitic fluid infection is the second most common complication in DCLD patients with the prevalence rate of 9-12% following UGI bleed, progressing to Hepatorenal syndrome and deaths. UGI bleed itself is an important risk factor the development of ascitic fluid infections by disrupting the mucosal barrier. The mortality rate in AFI and its complications ranges from 21-41%. So AFI is one of the treatable cause of death in DCLD patients.

Thorough knowledge regarding the pathogenesis, risk factors, microbiological profile and its resistance pattern is necessary to bring down the mortality rate associated with AFIs. AFI is diagnosed by ascitic fluid PMN count and culture which takes minimum of 3 days to get the culture report. So AFIs should be early identified and treated to avoid complications.

Mean Platelet Volume done early within 2 hours of patient presentation, which detects the inflammatory process due to the release of inflammatory markers like interleukins and its effects on platelet size.

During this study eligible patients with ascites were assessed after appropriate investigations. 75 patients were identified with ascites due to cirrhosis among inpatients and outpatients.

Most of the patients in our study population were in the age group of 41-50 years. Among the inpatients, most of them were in the age group of 51-60 years. The Mean age of presentation was 49.52 years. Median age was 50 years. There was a good correlation with the mean age in the studies ***Grunhage et al***[5] who had median age of 50 years. ***Dodammani et al***[22] had the similar median age group, ***Zahidulla et al***[71]who had population with the mean age group of 52.5 years.

Cirrhosis patients consisted of 68 (90.6%) men and 7 (9.3%) women. The most common cause of cirrhosis in male patients was ALCOHOLIC CIRRHOSIS 53 out of 75 (70.6%), 77.4% among inpatients and 65.9% among the outpatients. This correlated well with the study ***Pazhanivel et al***[51]and ***Grunhage et al***[5] where alcoholic cirrhosis was 57.5% and 64.5%.

All the outpatients were asymptomatic. Among the inpatients, the most common presenting symptom was abdominal pain with fever(58.6%) which correlated well with the studies ***Caruntu***[28](32%) and ***McHutchison***[48](68%)

In our study Leucocyte count was elevated to more than 12000 in11.36% of patients. Study conducted by ***Todd et al***[66] stated that there was subtle elevation of leucocyte count due to hypersplenism which was not correlated with our study.

ESR was significantly elevated to more than 30 in 96% of patients with AFI which correlated well with the study ***Suvak et al***[70] 90%

MPV was significantly elevated to more than 8.5 in 83% 0f patients with AFI which correlated well with the study ***Suvak et al***[70] . TC, ESR, MPV were all significantly elevated among the inpatients.

In our study, serum Bilirubin was elevated to more than 3mg% in 100% of patients with AFI and in all inpatients. The importance of this parameter as an independent risk factor had been ascertained by various studies ***Angeloni et al***[62]**,** ***Riberiet et al***[55] who confirmed this importance in their multivariate analysis.

Low serum Albumin less than 3.5gm% was found in our study in 93.1% of patients with AFI. S.Albumin forms the important factor in assessing CTP score. The significance of this parameter as an important risk factor was published in an article ***Erica Horinek***[24] .

In our study, serum Creatinine was elevated to more than 1mg% in 20.4% in inpatients and 17.2% in patients with AFI. Serum Creatinine was found as an independent risk factor for mortality in the study conducted by ***Lubna Kamani et al***[44] and ***Anastasiou et al***[34] in their multivariate analysis with a high statistical significance of(p=0.0098)

In our study, among the ascitic fluid infections, spontaneous bacterial peritonitis was present in 18 patients and monomicrobial non neutrocytic bacterascites was present in

11 patients. This had a good correlation with other studies like ***Pazhanivel et al***[51]and ***Riberiet et al***[55].

In our study, out of 18 patients having SBP, 9 patients had elevated Leucocyte count more than 11000 with peripheral neutrophilis of 60%. This showed that ascitic fluid neutrophil had good correlation with peripheral neutrophils. This observation was not correlated with study ***Angeloni et al***[62] which stated that PMN reaches the peritoneal fluid in response to specific stimuli and where there are ongoing local pathogenesis as stated by ***Mainor et al***[46].

In our study, among organisms that cause ascetic fluid infections, Gram negative bacilli was most common 96.1%. This had a good correlation with other studies ***Riberio et al***[55] where 80% was due to GNB and ***Rimola et al***[5]where 65% was due to GNB. All female patients were affected by GNB only.

In our study, MPV was correlated with various etiologies of cirrhosis. There was no statistical correlation even in patients with cirrhosis caused by Hepatitis B and C.

In our study, MPV had a good correlation with clinical features of abdominal pain 83.3% with a significant p value of 0.005 and of fever 78.1% with a significant p value of 0.005 , which states that MPV had been elevated in inflammatory conditions.

In our study, MPV was elevated in 88% of patients having TC between 4000 and 12000 % with a significant p value of 0.005. This observation had a good correlation with other study ***Suvak et al***[70] with a p value 0.001.

In our study, MPV was elevated in 68.4% having elevated ESR of more than 30 with a significant p value of 0.001. This observation had no correlation with previous study ***Suvak et al***[70].

In our study, MPV was elevated in 54.5% of patients having platelet count less than 100000 with a significant p value of 0.000.

In our study, MPV was elevated in 93.3% of patients having PMN count more than 250 cells/cu.mm with a significant p value of 0.000.This observation had good correlation with the study conducted by ***Suvak et al***[70].

In our study, MPV was elevated in 82.7% of patients with a positive ascitic fluid culture with a significant p value of 0.000.This observation had good correlation with the study conducted by ***Suvak et al***[70].

In our study, MPV was elevated in 93.3% of patients having PMN count more than 250cells/cu.mm and positive ascitic fluid culture with a significant p value of 0.000.

LIMITATIONS

- Ascitic fluid analysis should be done before starting empirical treatment for ascitic fluid infections, as even with first dose antibiotics PMN count will reduce to less than 250cells/cu.mm and culture may give false negative report.
- MPV should be done within 2 hours of blood sample collection, because it may give false positive MPV report due to cell swelling.
- Blood sample should sent with appropriate anticoagulant with appropriate dose, because it also gives false positive MPV report due to cell swelling.

CONFLICT OF INTEREST

Authors declare no conflict of interest related to this article.

CONCLUSION

- The prevalence of ascitic fluid infection among inpatients with DCLD is 65.9%
- The most common risk factor for the development of ascetic fluid infection among the inpatient is Alcoholism with the prevalence of 68.9%
- Ascitic fluid infection is the most common complication in DCLD patients. If untreated, it may lead to serious complications like Hepato renal syndrome and finally results in death. So, by identifying ascitic fluid infection early, we can reduce the mortality rate. The diagnostic criteria for ascitic fluid infection requires ascitic fluid PMN count and culture, of which ascitic fluid culture will take atleast 3 days to have a report. So, by measuring Mean Platelet Volume, a cheaper and non invasive method, we can diagnose ascitic fluid infection early and treat the patient at the earliest.

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PROFORMA

NAME : DIAGNOSIS:

AGE/SEX:

OCCUPATION:

ADDRESS:

DETAILS OF PRESENT ILLNESS:

ABDOMINAL DISTENTION

- Duration
- Course

ABDOMINAL PAIN

FEVER

PEDAL EDEMA

YELLOW COLOURED URINE AND SCLREA

ASSOCIATED COMPLAINTS:

- Decreased urine output
- Breathlesnsss
- Altered sensorium
- Hemetemesis , malena

PAST HISTORY: Jaundice, tattooing, Major trauma with blood transfusions .

FAMILY HISTORY: Jaundice, Hepatocellular Carcinoma, Cirrhosis.

PERSONAL HISTORY: Sleep,Diet, Smoking, Alcoholism,Drug abuse, Tobacco chewing,Sexual contact,

GENERAL EXAMINATION:

- Built & nourishment:
- Height: weight: BMI:
- P/I/CY/CL/LN/PE
- VITALS- PR.BP,RR,TEMPERATURE
- Signs of Liver cell failure

SYSTEMIC EXAMINATION

Abdomen

- Inspection :
- Palpation :
- Percussion :
- Auscultation:

❖ Cardiovascular system

❖ Respiratory system

❖ Abdominal system

INVESTIGATIONS:

- **CBC –** TC-

  DC-

  Platelets-

  Mean platelet volume-

  ESR-

- **BIOCHEMISTRY:-**

  LFT- T.Proteins

  Alb/Glb

  S.Bilirubin

  AST/ALT

  SAP

  RFT -B.Urea,

  S.Creatinine.,

  Serum electrolytes(Na, K, Ca)

- URINE ROUTINE EXAMINATION---sugar,albumin, deposits
- CHEST X-RAY
- ASCITIC FLUID ANALYSIS

  Alb

  T.Proteins.

  Cell count PMN

ASCITIC FLUID CULTURE

MASTER CHART

NAME	AGE	SEX	OP/IP	ALCOHOL	HBV	HCV	OTHERS	ABD.PAIN	FEVER	UGI BLEED	HE	DIARRHEA	HB(GM%)	TC	DC	ESR	PLATELETS	MPV	S.BILIRUBIN	AST	ALT	S.PROTEIN	S.ALBUMIN	S.GLB	PT INR	S.UREA	S.CREATINI	AF-PMN	AF-CULTURE
RAJI	58	M	IP	YES	NO	NO		YES	NO	NO	NO	NO	9.4	6400	68/30/2	40	78000	8.9	10.2	216	112	6	3.2	2.8	1.2	28	0.8	255	E.COLI
ELUMALAI	60	M	IP	YES	NO	NO		NO	YES	NO	NO	NO	9.2	9000	70/27/3	50	55000	8.6	8.6	200	112	5.6	3.6	2	1.6	32	0.7	244	K.PEUMONIAE
DELHIBABU	53	M	IP	YES	NO	NO		NO	YES	NO	NO	NO	8.9	8900	67/28/5	80	94000	8.9	14	198	94	6.2	3.6	2.1	1.4	24	1	200	E.COLI
MANI	46	M	OP	YES	NO	NO		NO	NO	NO	NO	NO	9.6	3700	70/28/2	10	112000	7.9	4.2	28	24	5.6	3.2	2.4	2	24	0.7	20	NO GROWTH
GUNASEKA	45	M	IP	YES	YES	NO		YES	YES	NO	NO	NO	8.8	10000	82/18/0	80	54000	8.8	6.8	98	94	6	3.5	2.5	0.9	30	0.9	260	K.PEUMONIAE
MOORTHY	38	M	IP	YES	NO	NO		NO	YES	NO	NO	NO	9	5900	68/30/3	24	62000	8	6.4	168	98	5.5	3.4	2.1	1.4	36	1	40	NO GROWTH
VENKATAC	45	M	OP	YES	NO	NO		NO	NO	NO	NO	NO	9.2	6000	65/33/2		125000	8.2	3	46	28	6.5	3.5	3	0.6	24	0.8	44	NO GROWTH
MALLIKA	46	F	IP	NO	YES	NO		YES	YES	NO	NO	NO	8.9	6600	72/28/0	64	72000	8.6	14	126	98	6	3	3	1.2	26	0.9	250	E.COLI
MARI	53	M	IP	YES	NO	NO		YES	NO	NO	NO	NO	8.8	4500	65/33/2	28	100000	8.2	9	136	88	5.8	3.4	2.4	0.9	28	0.7	22	NO GROWTH
BABU	44	M	OP	YES	NO	NO		NO	NO	NO	NO	NO	8	4200	64/34/2	10	115000	7.9	2.8	98	36	6	3.4	2.6	0.9	32	1	20	NO GROWTH
MARUTHA	69	M	IP	YES	NO	NO		NO	NO	YES	NO	NO	7	5100	60/38/2	28	94000	8	14	264	198	5.8	3.2	2.6	3	30	1.2	56	NO GROWTH
SADASIVAI	56	M	IP	YES	NO	NO		NO	NO	YES	YES	NO	7.2	4200	72/26/2	32	52000	8.2	9.8	196	94	6	3	3	2.8	28	1.1	50	NO GROWTH
SEKAR	55	M	IP	NO	NO	NO	CYPTOGEN	YES	YES	NO	NO	NO	8.4	16000	74/26/0	106	56000	9.2	12	77	98	5.6	3.2	2.4	0.9	39	1.5	400	P.AERUGENOSA
RAMESH	44	M	OP	YES	NO	NO		NO	NO	NO	NO	NO	9	4700	64/36/0	32	124000	8.4	2.4	36	24	6.2	3.2	3	1.3	30	1.2	10	NO GROWTH
PALANIVEL	46	M	OP	YES	YES	NO		NO	NO	NO	NO	NO	8.9	5000	68/30/2	20	123000	8.2	3	28	14	6.4	3.5	2.9	1.6	26	0.8	26	NO GROWTH
GANESAN	62	M	OP	YES	NO	NO		NO	NO	NO	NO	NO	8.6	6400	72/26/2	16	115000	08-Jan	3.8	32	18	6	3.5	2.5	0.9	32	1	22	NO GROWTH
KUMAR	48	M	IP	YES	NO	NO		YES	YES	NO	NO	YES	9	12000	80/18/2	94	58000	8.6	12.4	244	168	5.6	3	2.6	1.4	26	0.8	244	S.AUREUS
ROJA	36	F	IP	YES	NO	NO		NO	NO	YES	NO	NO	7.8	6000	70/27/3	30	48000	8.4	10	176	128	5.8	2.9	3.1	0.6	28	0.9	58	NO GROWTH
ATHIYAPPA	58	M	IP	NO	NO	NO	NAFLD	YES	YES	NO	NO	NO	9.2	12200	82/16/2	110	120000	9.5	5.6	30	28	6.5	3.5	3	1.5	36	1	256	ENTEROCOCCI FAECALS
MARI	60	M	IP	YES	NO	NO		YES	YES	NO	NO	NO	8.2	13000	82/17/1	112	66000	8.6	7	46	28	6.2	3.5	2.7	0.9	30	0.9	262	E.COLI
AHMED AF	54	M	IP	NO	YES	NO		NO	NO	YES	NO	NO	8.9	4500	68/30/3	44	94000	8.3	21	332	328	5.5	3	2.5	2.4	40	1.4	44	NO GROWTH
THANGAM	39	F	IP	NO	YES	NO		NO	NO	NO	YES	NO	8	6700	70/26/4	88	68000	8.2	14	446	428	6.2	3.5	2.7	1.6	32	0.7	56	NO GROWTH
ARUMUGA	58	M	OP	YES	NO	NO		NO	NO	NO	NO	NO	9.2	4000	62/38/0	14	136000	8.1	2.6	24	18	6.2	3.8	2.4	0.8	26	0.8	12	NO GROWTH
MARIAPPA	60	M	OP	YES	NO	NO		NO	NO	NO	NO	NO	9.4	5700	60/38/2	10	150000	8.4	1.8	22	16	6.8	3.8	3	1.1	23	0.8	20	NO GROWTH
ANNAMAL	54	M	OP	YES	NO	YES		NO	NO	NO	NO	NO	8.1	4400	54/42/6	18	124000	8.3	2	36	28	6.4	3.6	2.8	1.7	36	1	62	NO GROWTH
SENTHILKU	35	M	IP	YES	NO	NO		YES	YES	NO	NO	NO	7.8	12500	70/28/2	96	94000	8.8	8.6	156	112	5.5	3	2.5	1.9	35	1.2	310	K.PNEUMONIAE
THANGAVI	44	M	OP	YES	NO	NO		NO	NO	NO	NO	NO	8.2	5600	62/38/0	14	156000	8.4	3.2	34	28	6.6	3.5	3.1	1.6	28	0.7	34	NO GROWTH
SUMAN	38	M	IP	NO	NO	YES		YES	YES	NO	NO	NO	8.8	10000	72/24/4	64	98000	8.5	14	224	168	5.8	3	2.8	1.8	32	0.9	265	E.COLI
VADIVEL	57	M	OP	YES	NO	NO		NO	NO	NO	NO	NO	8.9	4300	66/30/4	18	10000	8.2	4	36	32	7	3.9	3.1	0.8	28	0.8	24	NO GROWTH
THANIGAC	59	M	IP	NO	NO	NO	CYPTOGEN	YES	YES	NO	NO	NO	9	7900	74/24/2	88	126000	9	8.8	168	189	5.8	2.9	2.1	1.9	30	1	340	P.AERUGINOSA
RAMASAM	54	M	OP	NO	YES	NO		NO	NO	NO	NO	NO	9.4	4800	58/40/2	14	136000	8.1	4.6	224	128	6	3.5	2.5	0.9	24	0.7	26	NO GROWTH
DINESH	38	M	IP	YES	NO	NO		YES	YES	NO	NO	YES	7.9	9800	80/18/2	88	68000	8.8	14.2	268	210	5.6	2.6	2	1.7	28	0.9	290	K.PNUMONIAE
ELLAPPAN	62	M	IP	YES	NO	NO		YES	YES	NO	NO	NO	9.4	12000	82/16/2	94	55000	8.7	18	112	98	6	3.6	2.4	1.2	26	0.7	265	P.MIRABILIS
MARIMUT	55	M	IP	YES	NO	NO		NO	NO	NO	YES	NO	8	5800	66/30/4	24	96000	8.1	16	198	124	5.6	2.9	2.7	1.6	29	0.7	50	NO GROWTH
PARAMASI	48	M	OP	NO	YES	NO		NO	NO	NO	NO	NO	8	4300	56/40/4	46	128000	8	3.2	32	28	7	3.7	2.3	0.7	32	0.8	42	NO GROWTH
THIYAGAR	39	M	IP	YES	NO	NO		YES	YES	NO	NO	NO	8.8	9800	76/24/0	86	100000	8.9	8.4	112	98	6	3.4	2.6	1.1	38	1	250	K.PNEMONIAE
LOGANATH	52	M	OP	YES	NO	NO		NO	NO	NO	NO	NO	8.9	4200	62/36/2	22	117000	8.2	4	30	24	6.6	3.7	2.9	1.3	27	0.8	32	NO GROWTH
RAMESH	40	M	OP	YES	NO	NO		NO	NO	NO	NO	NO	9	5100	60/36/4	26	145000	8	2.1	22	18	6.4	3.4	3	1.1	29	0.9	42	**NO GROWTH**
JOTHI	35	F	IP	NO	YES	NO		YES	YES	NO	NO	NO	9.2	12000	82/18/0	90	88000	9.4	6.8	132	98	5.8	2.9	2.9	1.2	34	1.1	500	P.MIRABILIS
SAMPATH	44	M	OP	YES	NO	NO		NO	NO	NO	NO	NO	9.8	5400	62/38/0	14	123000	8.4	1.8	26	24	6.4	3.8	2.6	0.9	28	0.9	34	NO GROWTH
ILAIYARAJA	39	M	IP	YES	NO	NO		NO	YES	YES	NO	NO	9.7	8400	70/26/4	94	78000	8.5	4.2	88	64	6	3.5	2.6	2.8	32	1.2	240	K.PNEUMONIAE
KATHIRVEL	51	M	OP	NO	YES	NO		NO	NO	NO	NO	NO	8.9	5000	64/30/6	18	148000	8	2	32	28	6.6	3.8	2.8	0.9	29	0.9	46	NO GROWTH
KAMARAJ	53	M	IP	YES	NO	NO		YES	YES	NO	NO	NO	8.6	10000	80/18/2	74	82000	9.2	7.8	138	98	5.9	3	2.9	1.2	28	0.8	356	K.PNEUMONIAE
MOHAN	39	M	OP	YES	NO	NO		NO	NO	NO	NO	NO	9.6	6500	66/32/2	16	146000	8.3	3.2	36	24	6.4	3.4	3	1.4	32	0.8	56	NO GROWTH
SIVAKUMA	40	M	IP	YES	NO	NO		NO	YES	NO	NO	NO	9.5	9800	76/22/2	40	100000	8.2	5.6	58	46	6	3	3	0.9	24	0.8	86	NO GROWTH
GOVINDHA	62	M	IP	NO	NO	NO	MALIGNAN	YES	NO	NO	NO	NO	7	5200	60/28/2	38	82000	8.4	12	236	240	5.6	3	2.6	1.5	34	1	48	NO GROWTH
JAYAKUMA	52	M	IP	NO	YES	NO		NO	NO	NO	YES	NO	9.7	5400	64/28/2	22	98000	8.3	16	238	224	5.8	3.3	2.5	1.6	32	0.9	134	E.COLI
ANAND	39	M	IP	YES	NO	NO		YES	YES	NO	NO	NO	9.6	12000	82/16/2	98	55000	9.1	24	198	126	5.5	3.2	3.3	0.9	28	0.8	476	P.MIRABILIS
TAMILARA	47	M	OP	YES	NO	NO		NO	NO	NO	NO	NO	9	4200	58/38/4	20	180000	8.3	2	18	12	6.8	4	2.8	1.2	34	1	22	NO GROWTH
KUPPAN	60	M	IP	YES	NO	NO		YES	YES	NO	NO	NO	8.9	9900	78/20/2	88	87000	8.5	9.4	126	88	6	3.6	2.4	0.8	28	0.8	120	E.COLI
NAGARAJ	56	M	IP	YES	NO	NO		NO	NO	YES	NO	NO	9.2	5600	66/30/4	24	64000	8.4	12	126	68	6.2	3.7	2.5	3.2	38	1.2	10	NO GROWTH
CHINNAPO	40	F	IP	NO	YES	NO		YES	YES	NO	NO	NO	7.4	9900	78/20/2	68	78000	8.6	18	234	198	5.6	3	2.6	0.6	23	0.8	NO CELLS	NO GROWTH
KARTHIKEY	36	M	OP	YES	NO	NO		NO	NO	NO	NO	NO	8.8	4300	60/28/2	22	134000	8.3	4	32	30	6.5	3.8	2.7	0.7	30	0.9	18	NO GROWTH
SUBBAIYAI	59	M	IP	YES	NO	NO		NO	YES	NO	NO	NO	8.2	8700	72/28/0	68	112000	8.5	6.6	164	98	6	3.5	2.5	1.3	28	0.8	NO CELLS	NO GROWTH
KARUPPAN	44	M	OP	YES	NO	NO		NO	NO	NO	NO	NO	9.9	4500	58/40/2	12	98000	8.2	4	42	34	6.2	3.8	2.4	0.8	34	0.9	26	NO GROWTH
SUBRAMA	53	M	IP	YES	NO	NO		NO	YES	NO	NO	NO	9.3	7600	56/40/4	64	68000	8.5	8.6	156	128	5.6	3.2	2.4	1.4	28	1	120	E.COLI
VELPANDI	52	M	OP	YES	NO	NO		NO	NO	NO	NO	NO	8.9	5400	66/30/4	22	150000	8	3.2	32	28	6.8	3.8	3	1.6	24	0.8	34	NO GROWTH
THANGAM	56	F	IP	NO	YES	NO		NO	YES	NO	NO	NO	7	6000	70/28/2	60	76000	8.6	7.8	156	94	5.4	3	2.4	3.6	29	0.9	134	E.COLI
NATARAJA	48	M	OP	NO	NO	NO	NAFLD	NO	NO	NO	NO	NO	9.9	4300	60/28/2	20	123000	8	2.8	22	18	6.9	3.6	3.3	1.9	28	0.7	22	NO GROWTH
MAYILVAG	59	M	OP	YES	NO	NO		NO	NO	NO	NO	NO	9.4	4200	64/32/4	14	156000	8.4	4.2	36	28	6.2	3.6	2.6	0.7	32	0.9	12	NO GROWTH
MANNAR	57	M	OP	YES	NO	NO		NO	NO	NO	NO	NO	8.3	5800	66/32/2	16	142000	8.2	3.8	44	26	6	3.5	2.5	1.3	28	0.8	NO CELLS	NO GROWTH
SUDDIN	36	M	IP	YES	NO	NO		NO	YES	NO	NO	NO	8.9	12000	80/18/2	80	54000	8.8	12.8	168	144	5.6	2.8	2.8	1.2	32	0.9	200	P.AERUGENOSA
PERUMAL	60	M	IP	YES	NO	NO		**NO**	YES	NO	NO	NO	9.8	12000	78/18/4	98	89000	9.8	14.6	188	134	5.8	3	2.8	1.9	24	0.9	256	K.PNEUMONIAE
PICHAI	58	M	IP	YES	NO	NO		YES	YES	NO	NO	NO	9	10000	82/18/0	68	78000	9	9.8	146	88	6	3.5	2.5	2	30	1	198	E.COLI
PERUNDEV	58	F	IP	NO	YES	NO		NO	NO	NO	YES	NO	7.4	6400	64/36/0	28	128000	8.5	7.8	66	44	5.4	2.9	2.3	1.5	28	0.8	32	NO GROWTH
SRINIVASN	39	M	OP	YES	NO	NO		NO	NO	NO	NO	NO	8.3	4200	56/40/4	12	153000	8.1	4	38	32	6	3.8	2.2	0.9	24	0.9	NO CELLS	NO GROWTH
MONSOOF	42	M	OP	YES	NO	NO		NO	NO	NO	NO	NO	9.8	4100	60/36/4	18	154000	8.2	3.2	24	18	6.4	3.6	2.8	1.4	32	1	10	NO GROWTH
RAMALING	48	M	IP	YES	NO	NO		YES	YES	NO	NO	NO	9.1	9000	78/28/2	66	78000	8.9	5.8	108	78	5.8	3	2.8	1.6	28	0.8	56	**NO GROWTH**
SETHURAM	49	M	OP	YES	NO	NO		NO	NO	NO	NO	NO	9.2	4000	66/30/4	20	121000	8.3	3	32	24	6.6	4	2.6	1.1	30	1	12	NO GROWTH
KRIHNAMO	40	M	OP	YES	YES	NO		NO	NO	NO	NO	NO	9.6	3800	64/36/0	18	98000	8.2	4	40	26	6.8	3.8	3	1	28	0.8	45	NO GROWTH
ARULANAN	39	M	IP	YES	NO	NO		YES	YES	NO	NO	NO	8.3	8700	78/28/4	76	65000	9	12.8	163	138	5.9	3	2.9	0.4	32	0.9	250	P.MIRABILIS
AMMAIAPI	57	M	OP	YES	NO	NO		NO	NO	NO	NO	NO	8.9	4100	64/30/6	16	127000	8.4	3.2	44	32	6.9	3.6	3.3	1.5	24	0.8	30	NO GROWTH
CHINNADU	62	M	OP	YES	NO	NO		NO	NO	NO	NO	**NO**	9	4300	66/32/2	22	99000	8.1	4.6	68	56	6	3	3	1.2	30	0.9	32	NO GROWTH
ARULNAM	41	M	IP	YES	NO	NO		NO	YES	NO	NO	NO	8.6	7800	80/20/0	68	86000	8.7	12.8	114	98	5.4	2.8	2.6	1.9	24	0.9	200	E.COLI
MANIVEL	56	M	IP	YES	NO	NO		YES	YES	NO	NO	NO	7.6	13000	90/10/0	126	96000	9	10.8	244	146	6	3	3	2	40	1.2	355	K.PNEUMONIAE

INSTITUTIONAL ETHICAL COMMITTEE
GOVT.KILPAUK MEDICAL COLLEGE,
CHENNAI-10
Ref.No.1589/ME-1/Ethics/2014 Dt:06.03.2014.
CERTIFICATE OF APPROVAL

The Institutional Ethical Committee of Govt. Kilpauk Medical College, Chennai reviewed and discussed the application for approval "AStudy on Mean platelet volume – An indicator of ascetic fluid infection in cirrhotic patients" – For Project Work submitted by Dr.S.V.Sangeetha, MD (GM), PG Student, KMC, Chennai-10.

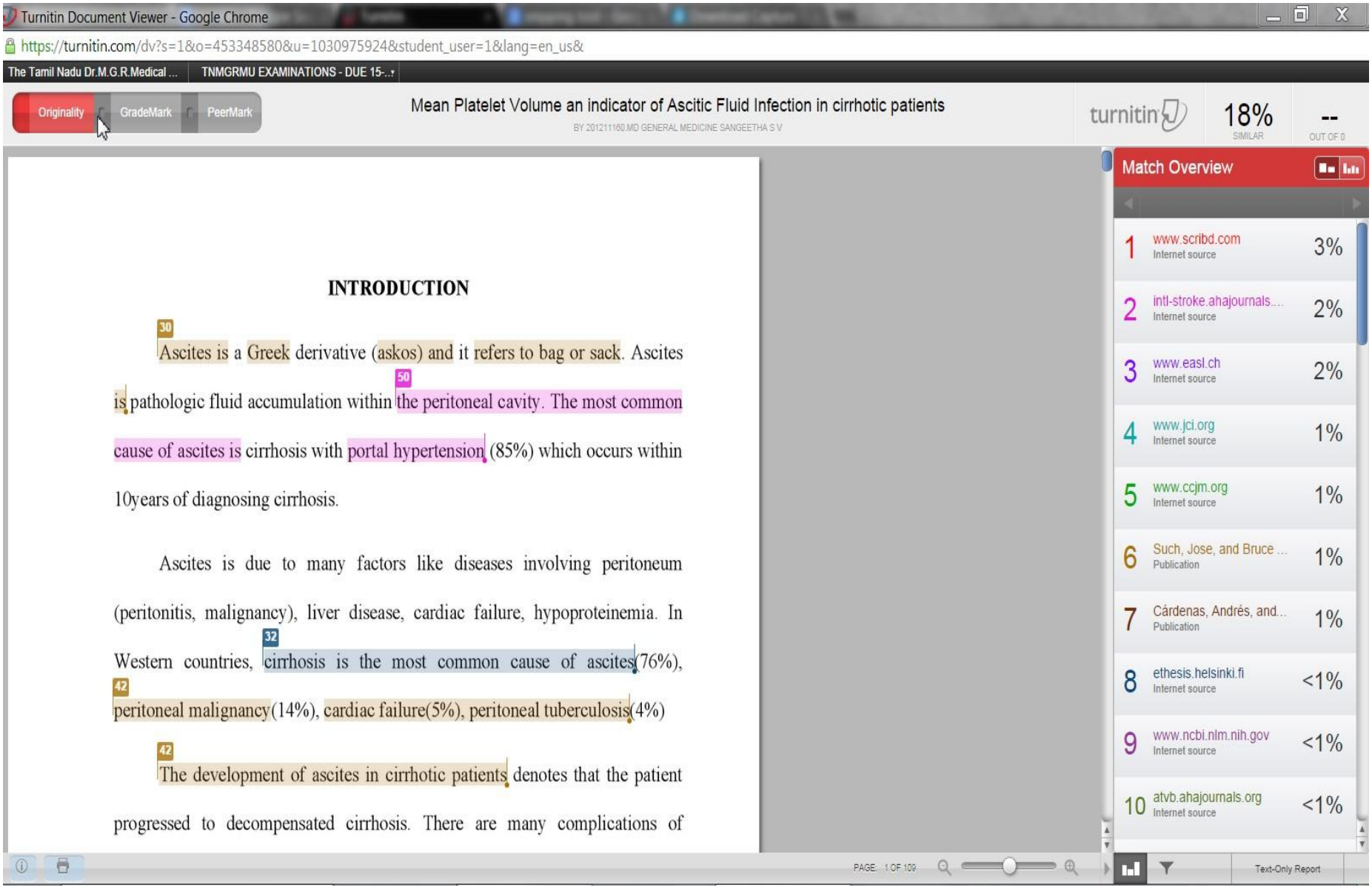
The Proposal is APPROVED.

The Institutional Ethical Committee expects to be informed about the progress of the study any Adverse Drug Reaction Occurring in the Course of the study any change in the protocol and patient information /informed consent and asks to be provided a copy of the final report.

29/5/14

CHAIRMAN,
Ethical Committee
Govt.Kilpauk Medical College,Chennai

GOVT. KILPAUK MEDICAL COLLEGE
29 MAY 2014
Kilpauk, Chennai-10.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INTRODUCTION
30
Ascites is a Greek derivative (askos) and it refers to bag or sack. Ascites is pathologic fluid accumulation within 50 the peritoneal cavity. The most common cause of ascites is cirrhosis with portal hypertension (85%) which occurs within 10years of diagnosing cirrhosis.
Ascites is due to many factors like diseases involving peritoneum (peritonitis, malignancy), liver disease, cardiac failure, hypoproteinemia. In Western countries, 32 cirrhosis is the most common cause of ascites(76%), 42 peritoneal malignancy(14%), cardiac failure(5%), peritoneal tuberculosis(4%)
42
The development of ascites in cirrhotic patients denotes that the patient progressed to decompensated cirrhosis. There are many complications of
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